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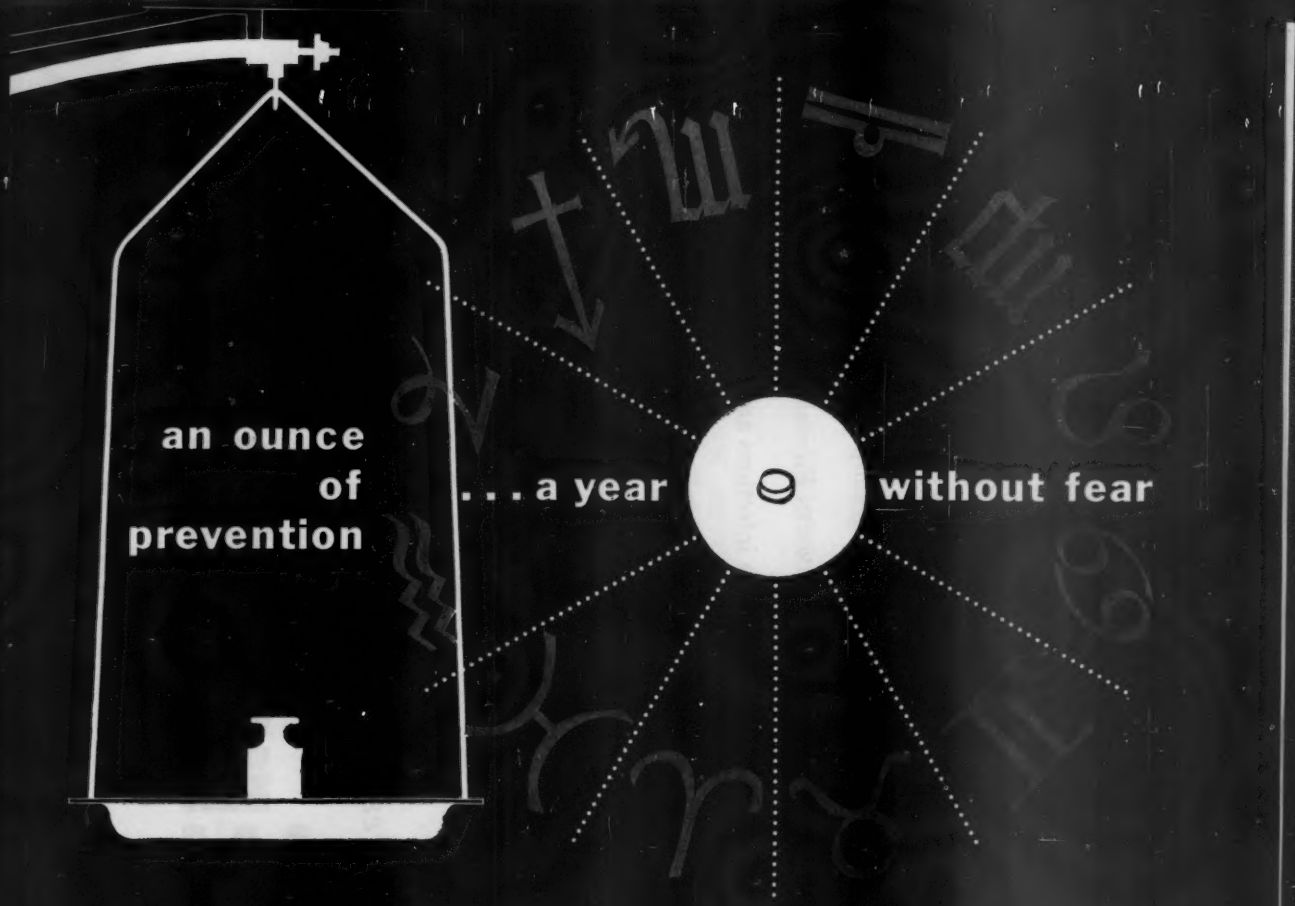

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1. Russek, H. I.; Urbach, K. F.; Doerner, A. A., and Zohman, B. L.: J.A.M.A. *153*:207 (Sept. 19) 1953. 2. Winsor, T., and Humphreys, P.: Angiology *3*:1 (Feb.) 1952. 3. Plotz, M.: New York State J. Med. *52*:2012 (Aug. 15) 1952.

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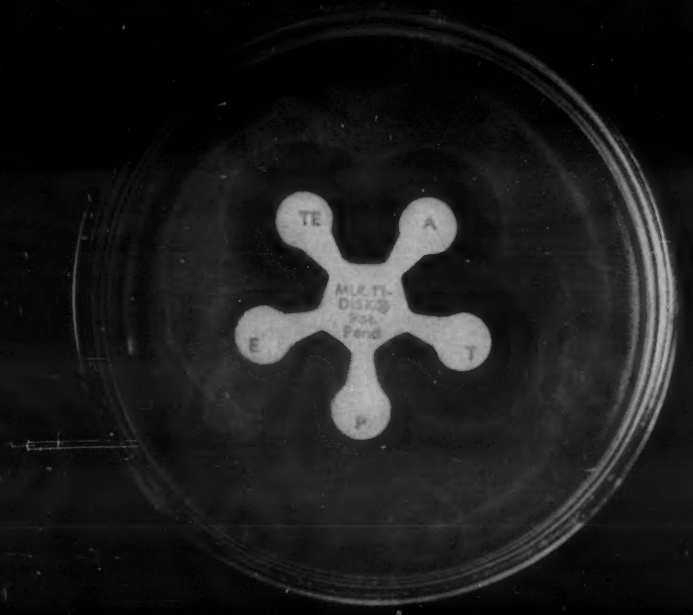

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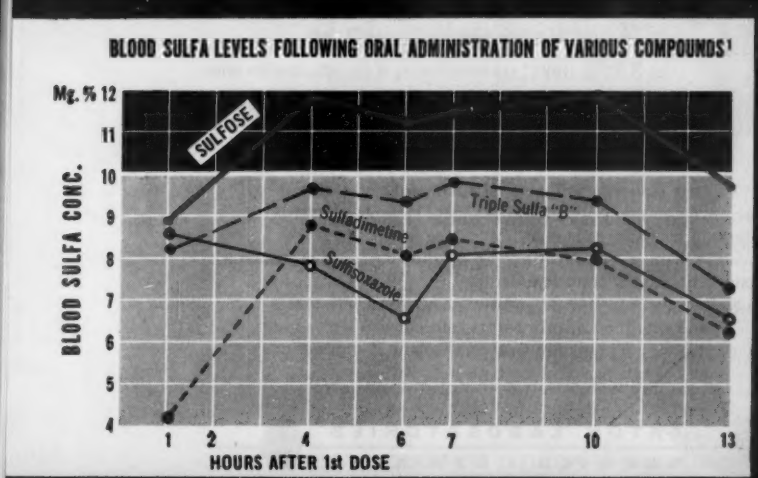

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1. Berkowitz, D.: Antibiot. & Chemo. 3:618 (June) 1953

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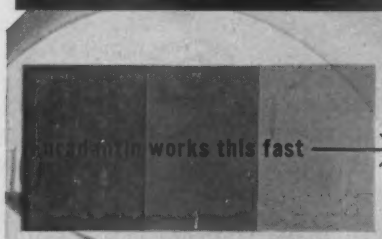

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1. MERLIS, S.: Diamox: A Carbonic Anhydrase Inhibitor—Its Use in Epilepsy. Neurology. 4:11, 863-866 November 1954.

2. BECKER, B.: Decrease in Intraocular Pressure in Man by a Carbonic Anhydrase Inhibitor, Diamox. Am. J. Ophth. 37:1, 13-15 January 1954.

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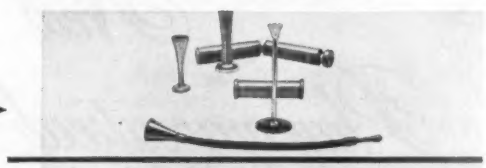

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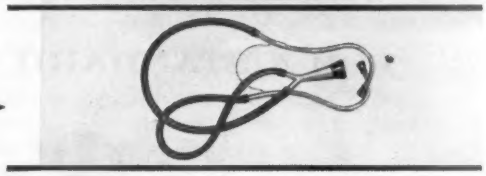

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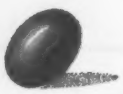

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Volume 252 FEBRUARY 10, 1955 Number 6

THE DIAGNOSIS AND MANAGEMENT OF BILIARY-TRACT DISEASE*

ROBERT M. ZOLLINGER, M.D.,† E. THOMAS BOLES, M.D.,‡ AND GLENN B. CRAWFORD, A.B.§

COLUMBUS, OHIO

THERE have been few fundamental contributions to the diagnosis and management of biliary-tract disease in recent years, but a current evaluation of the subject is justified in view of the large number of cholecystectomies being performed today and the frequency of complications of biliary-tract disease in patients seen by the surgeon for the first time. Cholecystectomy has become a common major abdominal operation, ranking approximately fourth after the triad of appendectomy, herniorrhaphy and hysterectomy. Although the operation is common, and the immediate morbidity and mortality are quite low, many patients tend to question the physician's recommendation for biliary-tract surgery. Even when they do not fear the operation, they harbor the idea that removal of the gall bladder will not ensure freedom from symptoms. The frequency of secondary biliary-tract operations lends support to the patient's suspicion and indicates the technical complexities of this procedure. The principles of management of biliary-tract disease, including the complications of acute cholecystitis and common-duct stone, that have proved satisfactory over a period of six years are presented.

DIAGNOSIS

Although the symptoms of chronic gall-bladder disease are well known and the accuracy of diagnosis by cholecystogram is quite high, in our experience over a third of the patients have one or more complications at the time of hospitalization. For example, in a six-year period, 1948 to 1953 inclusive, 676 patients were operated on for biliary-tract disease. In these cases common-duct calculi were found in 17 per cent, acute cholecystitis in 15 per cent, and pancreatitis, either alone or as a further complication, in 7 per cent. It is obvious that procrastination by the patient plays a large part in this situation, but since these complications are associated with an increased morbidity and mortality, physicians should evaluate their own responsibility in this regard.

The classic symptoms of gall-bladder disease are well known, although it is sometimes forgotten that high epigastric distress is the initial and at times the only type of pain associated with distention of the gall bladder or bile ducts by a calculus. Furthermore, if the block is sudden and complete, the diaphragm may be splinted, producing shortness of breath.[1,2] The occurrence of high epigastric pain, which at times may be substernal, combined with dyspnea in an obese, middle-aged person, offers a ready explanation for patients first regarded as having coronary insufficiency or occlusion who eventually prove to have only gall-bladder disease. The development of right-upper-quadrant pain may be delayed unless the gall bladder is acutely distended and in close proximity to the overlying peritoneum. Left-upper-quadrant pain is not rare and cannot be satisfactorily explained unless there is a proved associated pancreatitis. Blood amylase determinations should be made routinely in cases of gallstone colic because of the frequency of pancreatitis and the bizarre symptomatology that this complication produces. Unfortunately, the cholecystogram is of little value in the acute attack or in the presence of jaundice, although gallstones may be demonstrated by a scout film of the abdomen.

It is advisable for the physician to have a policy regarding the interpretation of the highly accurate cholecystogram as it is applied to the selection of patients for surgery. The positive demonstration of stones is the ideal finding on which to base a recommendation for operation. A single examination with nonvisualization is an inadequate criterion; this finding must be confirmed, by means of a reinforced dose of the dye, before surgery is warranted. The validity of the finding hinges on knowledge that the dye was taken by the patient and that its absorption was not altered by an acute gastrointestinal disturbance. Poor filling, delayed emptying and unusual size or shape of the gall bladder are not sufficient evidence of disease to merit operation. One must not read too much into the cholecystogram. On the other hand, the newer and more efficient drugs utilized in

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‡Assistant professor of surgery, Ohio State University College of Medicine.

§Research assistant, Department of Surgery, Ohio State University College of Medicine.

cholecystography may on rare occasions produce so dense a shadow as to hide small calculi. If the patient has had the classic symptoms of gallstone colic, the cholecystogram may be repeated and special technics used by the roentgenologist to show layering of the small calculi within the dye-filled gall bladder. Only in patients who have had repeated typical attacks of biliary colic is it justifiable to proceed with surgery despite an apparently normal cholecystogram. Gallstones should be recovered in almost every patient subjected to cholecystectomy if the best results are to be obtained.

Decision Regarding Operation

The presence of associated disorders may influence the decision for or against operation despite a classic history of gall-bladder disease and the proved presence of calculi by x-ray. Proof or suspicion of cardiac disease is a common reason given by patients as well as by too many physicians for delaying surgery. As previously mentioned, and as emphasized by Ravdin et al.,[3] it is well established that gall-bladder pain may mimic cardiac pain, and attacks of colic may intensify the severity of the heart disease. Experimental studies have shown definite cardiac arrhythmias after distention of the biliary tree, provided myocardial damage has previously been produced in the animals.[4] This is suggestive evidence to support the contention of most cardiologists that heart disease does not alter the surgical indications in recurrent gallstone colic, in suspected common-duct stone or in acute cholecystitis. These recommendations are not altered though the patient may have had a previous coronary thrombosis. It is not uncommon for a so-called "cardiac patient" to be completely relieved after the removal of gallstones. There is no more grateful group of patients, and the mortality and morbidity of biliary surgery are not particularly changed by the presence of proved cardiac disease.

Whereas the decision for or against surgery in the patient with severe cardiac disease may be difficult, there is less agreement about the recommendations to be made to the patient who has asymptomatic gallstones.[5-7] In evaluating the patient with "silent gallstones" one should consider how the gallstones were discovered and whether they are indeed asymptomatic or are producing atypical complaints. Were they found during the investigation of a patient's vague and bizarre intestinal complaints, or palpated during a pelvic laparotomy? Although this may be the era of preventive medicine, it is difficult for the patient to accept the risk and discomfort of surgery on the basis of a 50-50 chance of difficulty at some time in the dim future. Without sufficient proof, one's conscience does not permit discussion with the patient of the possibility that cancer will arise in a gall bladder that has been host to gallstones. On the other hand if the patient has had a duodenal ulcer or one or more attacks of pancreatitis, or has symptoms of recurrent cardiac origin, the removal of the gall bladder should be strongly advised. Obviously, it is not sound judgment to advise every patient with silent gallstones to have them removed irrespective of age or general physical condition. The age of the patient in relation to a life expectancy of approximately seventy years should be taken into consideration. A conservative attitude is justified in the older age groups, but a firm policy in favor of surgery should be taken for those under fifty years of age, since no one can predict which patient may develop one of the serious complications of gall-bladder disease twenty or thirty years later, when the risk of operation is obviously greater. Acute cholecystitis, obstruction of the common duct by a calculus and pancreatitis are the three most common complications that can be anticipated.

Acute Cholecystitis

The clinical diagnosis of acute cholecystitis justifies immediate hospitalization, since the subsequent course of the disease is unpredictable. Dehydration is corrected by appropriate intravenous infusion of fluids; nasogastric suction is instituted if vomiting continues, and Demerol and atropine are given for relief of pain. Although the inflammatory process is initially chemical, secondary bacterial invasion may occur sufficiently often to justify antibiotic therapy. Frequent repeated evaluations of the patient are essential in determining the response to the measures mentioned above. The abdominal findings, the white-cell count, the pulse and temperature chart and the narcotic requirement are correlated as frequently as every four hours in severe cases and less frequently in others until it can definitely be decided whether these conservative measures are bringing steady and sustained improvement, or whether surgery is necessary.

No matter how long the patient has had acute symptoms before hospitalization, it is the response to these universally applied conservative measures that determines the time of operation. If the physical findings, temperature, pulse rate and leukocytosis subside progressively after hydration, surgery is delayed until the patient is ambulatory and taking a full diet (Fig. 1). In this group, making up over 60 per cent of our patients, cholecystectomy is scheduled and performed several days or a week after admission to the hospital, in contrast to the policy of sending them home to return in several months for an elective procedure after the acute process has supposedly subsided.[8,9]

Approximately 20 per cent of the patients with acute cholecystitis either have an exacerbation of acute manifestations after an initial response or fail to improve from the onset. In general it has been our policy to operate on these patients as soon as hydration has been effected, usually within twenty-four hours of admission to the hospital. An early emergency off-schedule procedure has usually been per-

formed in patients in whom a flare-up develops after an initial favorable response.

A third group of patients with acute cholecystitis, comprising about 20 per cent of all cases, steadily worsen despite intensive conservative therapy. In this group the possibility of an impending or actual perforation of the gall bladder is to be considered because of the severity of the abdominal signs and symptoms. Failure of conservative therapy is much more frequent in this group. All such patients deserve surgical intervention as soon as they can be prepared for operation.

Although the cases of acute cholecystitis can be classified clinically in three groups, depending on the response to conservative measures, the time of operation divides them as follows: patients who can be deliberately added to the schedule for an elective operation, and those who should be scheduled, day, night, Sundays or holidays, for an emergency procedure at an off-schedule time. Obviously, those who fail to respond to the standard conservative measures fall into the latter classification. We are convinced that the mortality associated with acute cholecystitis can be held to a low and satisfactory level if the patients are operated on at any time, day or night, if they do not improve progressively under conservative management. An analysis of 103 cases of acute cholecystitis (1948-1953 inclusive) showed that all 20 patients whose disease progressed despite conservative therapy were subjected to an emergency off-schedule operation. Ten of the 22 with an exacerbation or failure to respond were similarly managed. The condition of the remaining 12 was satisfactory enough for surgery to be delayed and fitted in with the next morning's regular schedule. Not a single emergency operation was performed on the 61 patients who steadily improved under treatment. The feasibility of this simplified approach to the problem of acute cholecystitis seems justified, since only 1 death followed surgery in the 103 cases.

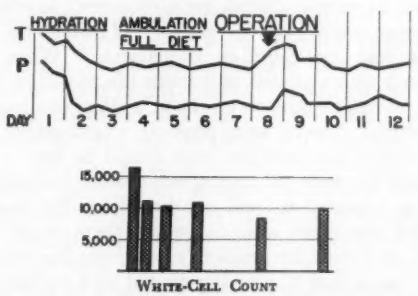

FIGURE 1. *Elective Cholecystectomy One Week after Admission in F.A., a Forty-Four-Year-Old Patient. The initial response to conservative measures was prompt and sustained.*

At operation in the majority of cases the distended gall bladder has been evacuated, the impacted calculus in the ampulla dislodged, and the gall bladder removed from the fundus downward. The dissection can be facilitated by developing a cleavage plane within the edematous wall of the acute gall bladder. Culture of the contents of the gall bladder should be taken. In 37 of the acute cases common-duct exploration was added to the procedure. The frequency of recovery of common-duct stones was 14 per cent of all cases in contrast to the over-all recovery rate of 17 per cent. Boyden[10] has recently called attention to the necessity of searching for common-duct stones in the presence of acute cholecystitis and reported a high recovery rate.

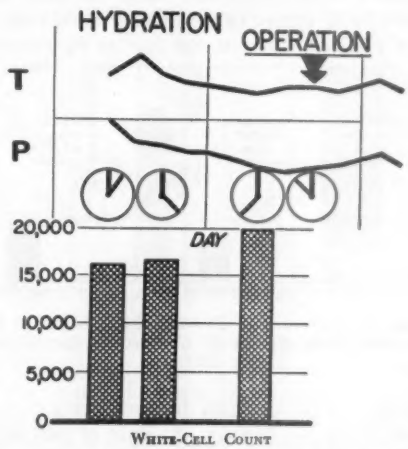

FIGURE 2. *Emergency Cholecystostomy after Hydration in an Eighty-Six-Year-Old Patient with Increasing Local Signs and a Rising Leukocytosis. The general condition was poor, and the duration of symptoms was three days. Some improvement was effected by hydration, but the disease progressed. Operation was performed twenty hours after admission.*

In 8.6 per cent cholecystostomy was performed. As advised by Ross and Dunphy,[11] we have, on occasion, deliberately planned a cholecystostomy under local anesthesia, especially in an elderly patient with an easily palpable mass (Fig. 2). On the other hand, more frequently the technical difficulties encountered at the time of surgery or the presence of a large abscess about the gall bladder properly influenced the judgment of the surgeon in favor of cholecystostomy.[12] Except in elderly or poor-risk patients, the gall bladder is later removed as an elective procedure.

COMMON-DUCT STONE

Autopsy and sporadic clinical reports during the past few years have suggested the presence of calculi in the common duct in approximately 20 per cent of all patients with cholelithiasis.[13,14] This, the most frequent complication of cholelithiasis, may be present and yet asymptomatic, may produce jaundice with its uncertainties of diagnosis, may block the pancreatic duct with resultant pancreatitis and, finally, may escape detection at the time of operation only

to plague the patient with recurrent symptoms and embarrass the surgeon who failed to remove it. Too frequently the possibility of common-duct stone is not entertained unless the patient has recently been jaundiced or is actually jaundiced at the time of operation. A survey of 100 patients in whom a stone was recovered from the common duct showed that only 2 in 5 were jaundiced at the time of surgery; 1 in 5 gave a past history of jaundice, and 2 in 5 had never been jaundiced.

Factors besides jaundice must therefore be depended on to ensure exploration of a sufficient number of common ducts at the time of operation. En-

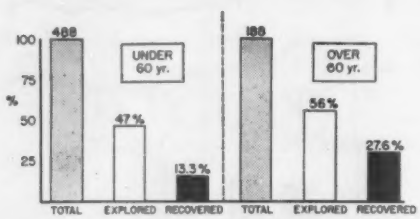

FIGURE 3. *Frequency of Common-Duct Calculi in Patients over Sixty Years of Age As Compared with Those under Sixty.*

largement of the common duct and cystic duct, small stones in the gall bladder, evidence of past or recent pancreatitis and secondary biliary-tract operations are indications for exploration of the common duct. If facilities are available for operative cholangiography, this procedure properly executed may decrease the frequency of common-duct exploration as well as ensure the discovery of any stones present or overlooked at the completion of the exploration.[15] For years we have followed the teachings of Cheever[16] regarding the technic of irrigating the ducts with small French woven catheters. The papilla of Vater is gently dilated by the use of these catheters in graded sizes, after which a small Cushing pituitary curette with flexible handle is passed upward and downward in a search for calculi. Gentleness is essential, especially during the procedure of irrigation through the catheter, because of the possibility of retrograde injection into the pancreatic duct, which may help the development of postoperative pancreatitis. Despite gentleness in the technical exploration of the common duct, postoperative pancreatitis was responsible for or was a major factor in 50 per cent of the 12 deaths during the past six years. Delicate, flexible instruments must be available for the performance of safe and efficient exploration of the common duct. Cholecystectomy should not be attempted unless the surgeon is prepared to explore the common duct, since exploration is necessary in a third to a half of all patients subjected to biliary-tract surgery. During the past six years (1948-1953 inclusive) we have explored the common duct in 43.8 per cent of the total cases, with an over-all mortality of 1.8 per cent.

The results of biliary-tract surgery might well be improved if every hospital, both large and small, made a yearly survey to determine among other things the recovery rate of common-duct stones in comparison to the probable ideal of approximately 20 per cent. In our experience overlooked common-duct stones are too frequent. For example, they were recovered in 35.5 per cent of all secondary operations carried out on the biliary system during the same six-year period. A study of the frequency of stones recovered in patients below sixty years of age as compared with those over sixty is of considerable interest (Fig. 3). The recovery rate of 27.6 per cent in the older age group was double that in the younger patients (13.3 per cent). These data suggest, as might have been expected, that the longer the patient has gallstones the greater the chance that stones will escape into the common duct. These findings lend strong support to the contention that gallstones, even asymptomatic, should be removed in those with the prospect of many years of life ahead of them.

JAUNDICE

Although jaundice is absent in many patients in whom a common-duct stone is recovered, in others its presence complicates the problem of differential diagnosis and preoperative preparation. When confronted with a jaundiced patient the physician should take sufficient time to arrive at a diagnosis based on a careful history and physical examination. The battery of liver-function tests should be used to confirm or disprove his clinical impression, but they cannot be expected to spell out the differential diagnosis. If the laboratory were diagnostic there would be no need to discuss the problem of determining which patient has a type of jaundice caused by a common-duct calculus in contrast to one due to hepatitis. A past history of gallbladder disease and a recent attack of colic followed by jaundice is the usual syndrome of a stone in the common duct. The jaundice may fluctuate and usually is not too intense. On the other hand the presence of two diseases must always be considered, and certainly surgery should be delayed in the jaundiced patient until the liver function has been evaluated and evidence for or against surgical versus medical correction of the jaundice assessed.[17] About half our mistakes in operations on jaundiced patients resulted from the fact that gallstones were proved by roentgenograms, and insufficient time was taken to evaluate the various laboratory tests, which eventually implicated clearly a hepatocellular type of jaundice rather than an extrahepatic blockage from the obvious gallstones.

If the various liver-function tests are to be evaluated, and we believe they should be, those favoring surgical correction of jaundice should be listed on one side of a balance sheet and those favoring medical correction of jaundice in the adjacent column. Fewer mistakes would be made if the data were tabulated

in this fashion on one sheet rather than listed at random on small laboratory reports, which in a puzzling case of jaundice may well approach 100 in number. We tend to delay surgery if the cephalin flocculation or thymol turbidity (or both) is elevated and if the prothrombin time cannot be raised above 50 per cent despite parenteral administration of vitamin K. If the cholesterol esters are below 50 per cent of normal or the serum mucoprotein level below 40 mg. per 100 cc. surgery should be postponed because of the strong probability of hepatocellular disease. If these tests are within the normal range but the alkaline phosphatase is elevated, the possibility of a stone in the common bile duct or carcinoma should be considered. The finding of a white stool and the persistence of jaundice longer than three or four weeks is sufficient evidence to recommend surgery in patients with a vague history combined with confusing or conflicting laboratory findings.

The time required for the determination and evaluation of the various laboratory procedures can be used to the patients' advantage if active steps are taken to improve their nutrition. The custom of almost routinely administering 10 per cent glucose intravenously to the jaundiced patient is satisfactory provided there has been sufficient emphasis on the oral intake. Every effort must be made to increase the patient's caloric oral intake regardless of possible distaste for food of any kind. Nasogastric-tube feedings of homogenized milk and bile, to which vitamins and other material may be added, is an economic and efficient method of preoperative preparation of the jaundiced patient. In addition, blood-volume determinations have shown a considerable deficit in many jaundiced patients, especially those who have lost weight (Fig. 4). The deficit was approximately 20 per cent in a series of patients with common-duct stone and 30 per cent in a small series with postoperative stricture of the common duct. Careful preoperative preparation of the jaundiced patient pays rich dividends and should not be bypassed, particularly in the older age group.

Technic

The reported frequency of strictures of the common duct suggests the need for more attention to the technical details of cholecystectomy.[18-20] There is no substitute for the proper positioning of the patient on the operating table, satisfactory relaxation, a liberal incision and exposure well illuminated into the depth of the wound. Time should be taken to mobilize the gall bladder into the field, with clear visualization of the region of the common duct.

Many surgeons find that as their experience increases they are removing more and more gall bladders from the fundus downward because of the added safety factor. In recent years we have preferred to incise the peritoneum along the entire inferior surface of the gall bladder about 1 cm. from the liver margin. The ampulla of the gall bladder should also be carefully dissected free of the common duct. After this an effort is made to peel the gall bladder from its bed until it tends to hang from the upper peritoneal attachment as if a mesentery had been developed. The cystic artery is then easily visualized from the under side of the gall bladder. It is tied, and the liver bed closed with interrupted sutures. Ordinarily, the liver margin is retracted as far into the wound as possible. After the liver bed is closed the liver margin is replaced into the peritoneal cavity and retracted upward by a Richardson retractor; this maneuver ensures a better exposure of the hepatic and common ducts. Consequently, a safer dissection of the entire cystic duct and subsequent exploration of the common duct is possible. It should never be forgotten that there are probably more normal anatomic variations in the region of the cystic duct than in any other zone of similar importance to the surgeon.[21] Those who accept the responsibility of biliary-tract surgery must be not only certain of their diagnosis but also secure in their technical approach to ensure safe and complete removal of all calculi whether located in the gall bladder, cystic duct or the intrahepatic ducts or impacted in the region of the papilla of Vater.

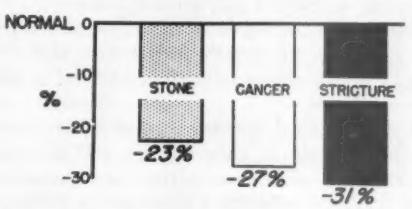

Figure 4. *Marked Preoperative Blood-Volume Deficits in Extrahepatic Obstructive Jaundice from Several Causes.*

Summary and Conclusions

The frequency of cholecystectomy today and the high prevalence of complications of biliary-tract disease found at the time of surgery justify an appraisal of the diagnostic criteria and the indications for operation in this disease.

The accuracy of diagnosis in gall-bladder disease is very high with the use of cholecystography. The demonstration of calculi is ideal, and nonvisualization, after proper confirmation, is satisfactory in the selection of patients for surgery; other findings, however, such as poor filling, abnormal size and shape and poor emptying, are not sufficient evidence of disease.

The recommendation of operation for patients with silent gallstones must be individualized, but is strongly urged in young and middle-aged patients. If gallstones are found in association with symptomatic cardiac disease, pancreatitis or duodenal ulcer, cholecystectomy is indicated as a general rule.

Patients with acute cholecystitis should be hospitalized, hydrated and closely observed. If the clinical course is one of continued and sustained improvement, operation is deferred until the patient is fully ambulatory and taking a normal diet. However, if the patient fails to improve on conservative measures, suffers a flare-up after initial improvement or has increasingly severe manifestations, an emergency, off-schedule operation is indicated.

The recovery of approximately twice as many common-duct calculi in patients over sixty years of age as in those under that age is compelling evidence for earlier surgery in gall-bladder disease.

Preoperative management of the jaundiced patient, with emphasis on dietary preparation and replacement of blood-volume deficits, is essential in assuring a low mortality.

In the technical performance of biliary-tract surgery, wide exposure, good lighting and adequate relaxation are essential requirements. A technic of cholecystectomy whereby a mesentery is developed on the upper, medial aspect of the gall bladder is briefly described.

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RUPTURE OF THE AORTIC VALVE*

A Therapeutic Approach

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RUPTURE of the aortic valve may occur as a result of trauma,[1-4] strain,[1,5] or bacterial infection.[6,7] The valves are usually the site of some predisposing factors such as rheumatic valvulitis, syphilitic infection,[6] atheromatous changes[1,6] and congenital anomalies.[4,8] Nevertheless, in a considerable number of cases, the valve, as seen at post-mortem examination, is otherwise normal.[1-4]

The feature common to free aortic insufficiency resulting from rupture, whether traumatic or infectious in origin, is the grave and usually hopeless prognosis.

Bright and Beck,[9] in 1935, reviewed the general subject of traumatic heart disease with a view of possibly salvaging some cases, and their studies resulted in a new approach to myocardial rupture. They concluded that it was necessary to observe closely for this complication as well as tamponade, and to institute immediate treatment by pericardial tap or, in certain cases, by actual suture of the myocardium. They excluded from analysis cases in which the injury produced a rupture of a valve without other manifestations of cardiac injury. "This group was excluded because a rupture of the valve seems to offer no possibility for operative repair."

Howard,[1] after reviewing 113 cases of rupture of the aortic valve was able to suggest only symptomatic measures in its treatment.

In 1951 Carroll,[6] discussing nontraumatic rupture of the aortic valve, stated that the emphasis must be placed on prevention of the underlying rheumatic and syphilitic heart disease "since little can be done

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for these patients once a rupture of the aortic valve has occurred."

Bean and Schmidt,[7] in 1953, reported the finding of disappearing diastolic blood pressure as an important sign in the diagnosis of rupture of the aortic valve due to endocarditis. At that time they asked, "Is there any use in being able to discover rupture of the aortic valve during life other than the clinician's pride?" In another article reporting rupture of the aortic valve caused by strain, Bean and Mohaupt[5] stated, "it is well to keep in mind the clinical picture of aortic valve rupture from strain, for the usually normal heart and the often normal valve present an ideal situation for surgical intervention." They further pointed out that "in these days of cardiac surgery it is well within the bounds of reason that operations may be devised that will correct the lesion acquired when an aortic cusp ruptures."

With the advent of surgical correction of aortic insufficiency by means of a plastic artificial valve, a ruptured aortic cusp can be successfully treated, and cases can be salvaged from what was formerly an almost certain rapidly fatal course. The following case of traumatic rupture of a previously normal aortic valve represents the first, to our knowledge, in which surgical correction was successfully employed.

Case Report*

A 17-year-old boy was admitted to Georgetown University Hospital with a chief complaint of "heart trouble" of 6 weeks' duration.

Six weeks previously, while assisting at the breeding of horses, he was kicked in the chest by the stallion. He remembered seeing the hind hoofs coming at him but had no recollection of being struck. Observers stated that he was knocked to the ground, but immediately arose with his hands clasped over his lower chest, took a few steps and then fell unconscious. He was taken to a nearby community hospital, where he was still unconscious on admission. Physical examination at that time was stated to have been negative except for abrasions over the anterior part of the chest. He had a lucid interval for a few moments on the night of admission during which he spoke to some friends and then lapsed into unconsciousness again. Forty-eight hours after admission, he regained consciousness and spoke in a rational manner but in retrospect had amnesia for the period from the time of injury until the 5th hospital day. On the 6th day, while watching the doctors examine him, he became aware of a noise in his chest, which he described as sounding like "a water pump leaking water around the valves." This noise seemed to be louder after activity such as sitting up in bed. He noted, in addition, a palpable thrill when he placed his hand over the precordium. During the 4 weeks of bed rest in the hospital he was symptom free except for an episode of lightheadedness while he was sitting up on a litter. Six weeks after the accident he was transferred to Georgetown University Hospital for possible surgical intervention.

The past history revealed no family or personal history of rheumatic fever or rheumatic heart disease and no history of congenital heart disease. He had always been an active youth, playing high-school varsity basketball without symptoms. An x-ray examination of the chest had been negative 3 years before admission, and a physical examination, including auscultation of the heart about 6 months previously had revealed no abnormality.

Physical examination showed a slender lad in no acute distress.

*We are indebted to Dr. E. A. Rasberry, Wilson, North Carolina, and Dr. Ernest Craige, Department of Medicine, University of North Carolina, Chapel Hill, for referral of this case.

The blood pressure ranged between 100/36 and 120/50 in the upper extremities and 160/40 and 180/50 in the lower extremities, the pulse between 80 and 90, and the respirations between 20 and 24.

The pertinent physical findings included striking expansile pulsation of the carotid neck vessels typical of free aortic regurgitation and a diffuse prominent apical impulse seen and felt over the entire precordium on the left, with transmission to the right side of the chest. The precordial heave was followed by a double thrust, and a thrill along the left sternal border was felt throughout diastole. Auscultation revealed a Grade 5 high-pitched musical diastolic murmur heard best along the left sternal border at the 3d interspace. A Grade 2 systolic murmur was present in the same area. At the apex a Grade 3 systolic murmur, a prominent Flint murmur and diastolic ventricular gallop were heard. Other signs of aortic insufficiency were a Quincke pulse and a Corrigan pulse. A pistol-shot sound was heard over the precordium as well as the femoral arteries and other peripheral arteries. A pulsus alternans was present.

Urinalysis was negative. A hemogram and the blood chemical constituents were normal. A serologic test for syphilis was negative.

The venous pressure on admission was equivalent to 196 mm. of saline solution, with a rise to 256 mm. on right-upper-quadrant pressure. The vital capacity was 2.8 liters on 2 measurements.

An electrocardiogram showed sinus tachycardia and incomplete right-bundle-branch block.

X-ray study demonstrated cardiomegaly with enlargement of the left ventricle of moderate degree. Cardiac catheterization revealed a significant increase in the oxygen content of the blood in the right ventricle over that in the right atrium.

It was believed that the patient had sustained a traumatic rupture of a normal aortic valve as evidenced by the classic cardiac findings and peripheral signs. In addition it seemed likely that a tear had involved the interventricular septum as indicated by the increased oxygen content of the blood in the right ventricle over that in the right atrium. The aortic insufficiency was considered the primary pathologic process. Since severe aortic insufficiency of this type usually carries a grave prognosis, with a rapidly fatal course over a period of a few months, it was decided to attack the problem surgically in an effort to arrest its natural progress. He was digitalized, placed on a low-salt diet and given mercurial diuretics on 2 occasions. Operation was performed 3 weeks later.

After the chest was opened the aortic valve was explored manually from the exterior, and a strong thrill could be felt over the area. No thrill was felt over either atrium. A plastic aortic valve was inserted in the 1st part of the descending aorta.[10-12] Postoperatively, the patient did not respond as well as the usual patient undergoing this operation in that he had nausea and vomiting for 1 week and a persistent sinus tachycardia, with a rate of 110 to 124, for 2 weeks. After operation the aortic diastolic murmur definitely diminished in intensity and duration. It was particularly striking that the loud murmur formerly heard throughout the diastole was now audible for only a short interval after the 2d sound. The Flint murmur disappeared, but the ventricular diastolic gallop persisted, though decreased in intensity. The blood pressure in the lower extremities, formerly 180/40, ranged between 115/75 and 125/85; the venous pressure dropped from 196 to 122 mm. of saline solution. Electrocardiograms continued to show incomplete right-bundle-branch block. Postoperative cardiac catheterization confirmed the preoperative findings by demonstrating an increase of 2.5 vol. per cent in the oxygen content of the blood between the right atrium and the right ventricle, further supporting the preoperative diagnosis of a tear in the interventricular septum in addition to the valvular lesion (Fig. 1).

The patient improved progressively, and 1 month after operation was discharged home for further convalescence and has since been asymptomatic. Fourteen months after operation he was working as a truck driver although he did no loading and unloading. X-ray study of the chest showed no significant changes in the cardiac silhouette.

The electrocardiogram was unchanged, the incomplete right-bundle-branch block persisting. Venous pressure 6 months after operation was equivalent to 130 mm. of saline solution, with no significant rise on right-upper-quadrant

pressure. The circulation time (measured with Decholin) was 11 seconds.

Discussion

Review of the Literature

The first case of rupture of the normal aortic valve was reported by Plenderleath[13] in 1820. Howard,[1] in

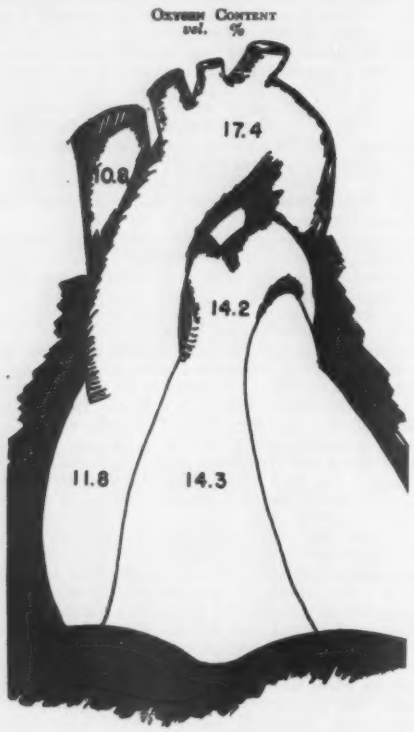

Figure 1. *Results of Postoperative Cardiac Catheterization. Note the significant rise in oxygen content between the right atrium and the right ventricle, evidence of a left-to-right intracardiac shunt.*

1928, reviewed the world literature and added a case of his own. The aggregate was 114 cases of rupture of the aortic valve, of which 47 were due to trauma other than "strain." Of the patients examined after death only 6 had otherwise absolutely normal aortic valves. Since that time 3 additional cases of traumatic rupture of the normal aortic valve have been described,[2-4] all diagnosed clinically and proved at autopsy.

Tears have been produced in the normal aortic valves of cadavers by the application of blunt force over the precordium.[14] The results have been reproduced in dogs.[15] Other investigations have shown that an increase in the intra-aortic pressure to levels ranging from 116 to 484 mm. of mercury frequently results in rupture of the aortic cusps.[16] This observation is supported by case reports of myocardial rupture caused by sudden application of pressure or compression of large areas of the body although the thorax itself was spared.[9,17] Thus, sudden compression may result in a steep rise in intra-aortic pressure with tearing of the valve.

Etiology

Clinically, most of these cases have resulted from powerful force transmitted to the chest wall by a blow, a fall, a kick or sudden compression or constriction. Many of the reported cases of rupture of the myocardium,[9] the interventricular septum[18] and the aortic valve[1] have, as in the case presented above, resulted from the kick of a horse.

Clinical Picture

Aortic insufficiency on the basis of a ruptured cusp does not differ essentially from the insufficiency from other causes except for the more rapidly fatal course. The patient frequently experiences a sudden, excruciating pain as if something had snapped or torn loose inside him; this is probably caused by the sudden dilatation of the heart and stretching of the pericardium, owing to the actual rupture. Other patients have immediate fatal syncope, or are unconscious for hours to days. On regaining consciousness, the patient may immediately become aware of a "roaring," "buzzing" or "humming" sensation in his chest that may, indeed, be audible not only to him but to others near him.[1,19] Our patient described quite correctly the sound coming from the anterior part of his chest as similar to that of a pump that is leaking around the valves. It is interesting that he confirmed his impression by palpating the thrill over his precordium.

The diastolic murmur of aortic-valve rupture commonly has a musical quality. It has been described as a "cooing-dove," "sea-gull" or "spinning-top" murmur. Such a loud musical murmur is not pathognomonic of rupture from trauma, nor is such a murmur present in every case.

Probably the most common cause of a musical aortic diastolic murmur is the eversion of the right anterior aortic cusp in the course of syphilitic disease of the aortic valve.[20] Rupture or destruction of the valve during bacterial endocarditis is next in frequency.[21]

These two conditions, in addition to traumatic rupture, are responsible for most musical diastolic murmurs and represent what is called acute aortic insufficiency — that is, the sudden appearance of free regurgitation in a previously normal or nearly normal heart or a sudden augmentation in the severity of the insufficiency formerly present. They are grouped together because they share the same poor prognosis[20] and therapeutic implications.

The observation, by Bean and Schmidt,[7] of the progressive lowering and disappearance of the diastolic pressure as a diagnostic sign of aortic-valve de-

struction in subacute bacterial endocarditis has been confirmed by one of us (J. J. L.).

It is well to remember that in severe aortic insufficiency due to rupture of the valve an apical rumble may be heard that represents the Flint murmur. Misconstruing this as the rumble of mitral stenosis would lead one mistakingly to assign such a double valvular lesion to rheumatic involvement in spite of a history of trauma.

Traumatic Rupture of the Interventricular Septum

The results of cardiac catheterization in this case proved interesting. The postoperative confirmation of the preoperative catheterization results (namely, the increase in the oxygen content between the right atrium and the right ventricle)* leave little doubt that a left-to-right shunt was present. Such a condition could result from trauma by one of two mechanisms. In the first place the tear in the area of the aortic ring may have extended into the sinus of Valsalva, with rupture of this sinus into the right ventricle. Such a sequence of events has never to our knowledge been reported secondary to trauma, although congenital aneurysms of the sinus may rupture, with perforation, as may lesions caused by bacterial endocarditis.[22] The second and more likely explanation is that the interventricular septum was ruptured since diastolic-pressure readings in the right ventricle (12 mm. of mercury) seemed to rule out the former condition as an isolated defect.

Isolated traumatic rupture of the interventricular septum because of blunt force has been reported in 13 cases.[18] Most of these ruptures are at the base of the septum although they may occur at any location and may be multiple. The size of the tear may vary from very small areas, which are discovered only by careful examination of the heart at autopsy, to large rents, which are obviously hemodynamically significant. The characteristic physical findings of congenital defect of the interventricular septum are present, consisting of a harsh systolic murmur at the fourth to the fifth interspace, along the left sternal border and sometimes accompanied by a thrill. If the defect is over 2 cm. in diameter a diastolic murmur may be present owing either to the lesion or to secondary pulmonary insufficiency. Large rents may take place in the absence of auscultatory findings. The classic clinical picture of rupture secondary to myocardial infarction[23,24] has many features in common with traumatic rupture. Both may occur not with the initial insult but hours to days later when the bruised or infarcted area undergoes softening. Both usually appear at the base of the septum, but whereas rupture secondary to apical myocardial infarction is almost always too small to cause any hemodynamic alteration, rupture due to trauma may be accompanied by sudden onset of pulmonary congestion[18] and later right-sided heart failure. In the case reported above, the diagnosis could not have been made without catheterization since the clinical features and cardiovascular alterations were overshadowed by the free aortic insufficiency.

*We are indebted to Drs. Edward Freis, Edward Partenope and Lawrence Lilienfield for these studies.

Prognosis

The sudden tearing of the aortic-valve cusps, with resultant free insufficiency, has a strikingly different clinical course from regurgitation on the basis of slowly progressive valvular incompetence due to disease. In laboratory animals extirpation of the valve leaflets results in sudden dilatation of the heart and immediate death or fulminating failure of the left ventricle with a progressively fatal course.

Since, clinically, rupture of the aortic valve may result in variable degrees of regurgitation, the prognosis is also variable. In Howard's[1] series 1 patient died immediately, another in two hours, a third in several hours, and still another in three days. At the other end of the scale 2 patients in this series lived for ten and eleven years respectively; we have attempted to determine how hemodynamically significant the insufficiency was in these 2 cases.

The patient who lived for eleven years, described by Steinitz[25] in 1910, was found at post-mortem examination to have a defect, 1 cm. by 2 cm. in diameter, in one of the aortic cusps. This was fairly well established to have occurred eleven years previously after a fall. The clue to the benign course in this case of rupture of the aortic-valve cusp lies in the blood-pressure reading on admission just before death. The systolic pressure was 165, and the diastolic 120. Our clinical experience with aortic insufficiency[12] indicates that a diastolic pressure of 120 would rule out severe aortic insufficiency. Yet it is easy to understand from Steinitz's diagram of the perforated cusp how a loud murmur could be present both in systole and in diastole as a result of the lesion.

The case report of a patient who lived for ten years was that of Barié,[26] who discussed Potain's case. The patient was a professional jockey who had had two severe falls from his horse, one ten years and one seven years before death. Both accidents resulted in chest pain, and the patient obviously had heart disease with angina at that time. On admission before death he had by description severe aortic insufficiency although blood pressures were not determined. This admission apparently was the first time his aortic insufficiency had been documented by careful physical examination. At post-mortem study endocarditis involving both the mitral and the aortic valves was described and, in addition, a tear in one of the aortic cusps. One cannot be sure whether the tear of this diseased valve resulted from trauma seven or ten years before death or was spontaneous, occurring at a later date.

The 2 patients in the reports of Kissane et al.[2,3] lived for fourteen and twenty-seven months after trauma, whereas the patient described by Bushong[4]

died after sixty-nine days. Carroll,[6] in his presentation of nontraumatic aortic-valve rupture, highlighted the poor prognosis by showing that 8 of 9 patients were dead in eight months. These investigations all point to the fact that free aortic insufficiency caused by rupture of the valve, regardless of etiology, usually results in rapid deterioration and early death. In the case reported above the presence of a severe aortic insufficiency, as manifested by classic peripheral signs and physical findings, suggests that the life expectancy would be a matter of months. Nevertheless, fourteen months after operation, the patient was symptom free and able to do a full day's work as a truck driver. This fact alone indicates a new era in the field of aortic-valve rupture. The diagnosis of these cases becomes more than an academic exercise because aortic-valve rupture may now be classified as a reversible or partially curable form of heart disease. Probably in the near future it may be completely curable.

Traumatic heart disease in general and valvular rupture in particular have always been more common than generally appreciated. In this day of rapid transportation by automobile, as well as airplane, these cardiac injuries will undoubtedly be seen more frequently. In addition the following sequence of events is becoming a common experience on the medical wards: a patient with rheumatic aortic insufficiency, minimal in severity, with little or nothing in the way of symptoms or incapacity, contracts bacterial endocarditis and, after five to eight weeks of treatment, is shown by repeated cultures to represent a bacteriologic cure; however, in the meantime, he shows the picture of overwhelming aortic insufficiency and deteriorates rapidly from progressive congestive heart failure, the minimal valvular incompetence having been replaced by severe insufficiency because of rapid destruction of the aortic valve. Here, again, the myocardium may previously have been normal or nearly normal. It is now the physician's responsibility to be able to diagnose such cases clinically because of the possibly life-saving therapeutic implications.

It follows that the physician must now be familiar with the prevalence and features of aortic-valve rupture so that early and accurate diagnosis may result in arresting this progressive disability and thereby prevent the early death that is the natural outcome.

Summary

A case of traumatic rupture of the aortic valve is reported. In addition the patient probably sustained a rupture of the interventricular septum as shown by two cardiac catheterization studies. Because of the poor prognosis in sudden free aortic insufficiency, both traumatic and nontraumatic, an artificial aortic valve was inserted in the descending aorta. Fourteen months after operation the patient was symptom free and working full time as a truck driver.

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SPORADIC (PERIODIC) PARALYSIS*

Report of a Case

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GRAND FORKS, NORTH DAKOTA

PERIODIC paralysis is a disease that, though infrequently seen, has been of much interest to the medical profession since it was first described by Cavaré[1] a century ago. Although it is usually thought of in terms of hereditary (familial) periodic paralysis, it seems advisable to follow Talbott's[2] suggestion of considering the clinical picture as a clinical syndrome that is variously hereditary (familial), sporadic or associated with other diseases (such as hyperthyroidism, malaria, nephritis and toxicity secondary to therapy with corticosteroid hormones). There is no essential difference in these three variations of the clinical syndrome though in about 80 per cent of the reported cases a definite familial occurrence can be traced.

Talbott,[2] in his excellent review of the subject in 1941, recorded a total of 400 cases in the literature up to that date. In addition he stated that 35 deaths in the same group were attributable to the disease, an over-all mortality of a little less than 10 per cent. Deaths have been reported by others since then,[3] as well as a high rate of infant mortality in a family described by Bickerstaff.[4] Thus, although this syndrome is relatively rare, the mortality is high enough to make early diagnosis and treatment mandatory.

The syndrome of periodic paralysis has the following clinical characteristics: recurrent episodes of flaccid muscular paralysis; depression or loss of deep reflexes; loss of excitability to electric stimulation of nerves and muscles; normal sensory perception; retention of consciousness, without alteration of sensorium during episodes; depression of serum potassium during attack; and cessation or relief of the attack after potassium therapy.

Typically, the paralysis begins in the early hours of the morning, the patient waking to find that he is unable to move. At other times attacks may be precipitated by exposure to cold, excessive physical exertion, emotional excitement or ingestion of a high-carbohydrate diet. Some patients may have prodromal warnings sufficient to enable them to stave off an attack by vigorous exercise. The paralytic attack usually involves only skeletal muscle; smooth muscle and muscles supplied by the cranial nerves remain normal. Thus, the muscles of phonation, deglutition and sphincter control are usually unaffected, though respiration may be embarrassed enough to necessitate mechanical aids as a life-saving measure.[5] Most commonly the paralysis begins peripherally and progresses centrally; it occurs in the upper, lower or all extremities, and may be unilateral or bilateral and either partial or complete. Attacks on the average last six to eight hours but may last three or four days, and they have been reported as lasting as long as seven or eight days. Frequency varies considerably from case to case, episodes being as far apart as ten years to the other extreme of several times per day. The sex prevalence runs about 3 males to 1 female in the familial group; the number of females in the sporadic group is very small. Usually, the disease develops in the first or second decade of life, but it has been reported in the first few months of life and coming on as late as fifty-six years of age. Frequently, the attacks decrease in middle life and disappear in late adulthood.

The striking laboratory change that has been described as characteristic of this disease is hypopotassemia during the acute paralytic attack. Though the beneficial effect of potassium salts was noted as early as 1901, Biemond and Daniels,[6] in 1934, first observed the low serum potassium during spontaneous attacks. However, the persistent relation of disturbed potassium metabolism as a factor in pathogenesis of the acute attack was not fully appreciated until two or three years later, when others were able to confirm these findings and also to demonstrate the prompt beneficial effect of potassium given either orally or parenterally.[7,8] Since that time these findings have been confirmed repeatedly. In recent years electrocardiographic studies during the paralytic attack have frequently been reported as showing changes typical of those described as occurring in hypopotassemia. However, just as the electrocardiographic changes are not directly correlated with the serum potassium level at any time, the serum potassium level in periodic paralysis bears no direct constant relation to the onset or cessation of paralysis. As a matter of fact there are several well documented, apparently clinically typical cases in which paralysis occurred in spite of a normal serum potassium level and in which potassium therapy was not effective in terminating or controlling the attack.[9-11]

With the knowledge that in some patients paralytic attacks could be precipitated by high doses of glucose by mouth, epinephrine given parenterally or glucose administered orally in combination with injection of insulin, several investigators have been able to follow other changes through more detailed studies of metabolic balance. The fact has been conclusively established that there is no additional excretion of

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potassium from the body before or during the acute paralytic attack. Actually, it has been shown that there is a decreased urinary excretion at that time.[12-15] Gammon et al.[16] produced a paralytic attack in a patient by water diuresis, with additional loss of potassium in the urine, but this appears to have been a unique experience. Several reports confirm a decreased serum phosphatase level during attacks but hasten to add that this is not proportional to the change in serum potassium.[8,14] Increased creatinine and urinary excretion has also been described and probably reflects only abnormal muscular metabolism.[12,14,15] A few observers have reported slightly elevated blood sugar levels, but the extent and number have not been noteworthy; those who have done glucose tolerance tests have found them to be normal.[7,9,14]

A natural conclusion from these facts is that before and during the acute attack of periodic paralysis there is a release of potassium from the blood stream that must be carried out by transfer of potassium from extracellular fluid to some other body tissue, presumably muscle cells.[17] The mechanism behind such a transfer is not clear, but evidence exists to point to the process of glycogenesis and resulting diversion of potassium ions as one factor in this peculiar defect of cellular physiology. An increase in potassium concentration in the muscle during the paralytic attack as compared to the asymptomatic interval has been reported, but further investigations have given conflicting results.[14,18,19] One must remember in discussing the role of potassium in periodic paralysis that all patients with hypopotassemia do not experience paralytic episodes. Although muscular weakness may occur in such situations, paralysis is quite rare. Of further interest in this regard are the numerous well documented cases of periodic paralysis in association with hyperthyroidism. Almost invariably these have also been associated with hypopotassemia, and the syndrome of periodic paralysis has been completely eradicated by adequate therapy of the hyperthyroidism.[20-22]

The data cited above suggest a basic metabolic defect in the susceptible person that, in most cases, is inherited, in others occurs idiopathically and in still others is only brought out by the occurrence of hyperthyroidism or some other metabolic change. That the location of this defect is in the muscle cell is assumed by most investigators though a central-nervous-system mechanism has also been hypothesized.

McQuarrie and Ziegler[19,23,24] showed clearly in one group of patients that attacks can be controlled by suitable diet in which the carbohydrate-potassium ratio has been well established. They pointed out that a high-fat, medium-protein, restricted-carbohydrate diet was just as deleterious as a high-carbohydrate diet in precipitating attacks.

The following case of sporadic periodic paralysis is considered to present several unusual features of special interest to the problem as a whole.

Case Report

A 58-year-old farmer was first seen on January 6, 1954, complaining of pain and weakness in both thighs, the right calf and, to a lesser extent, both shoulders, all of which had been present for 1 week. This pain was dull and aching, aggravated by motion of the extremity and relieved by rest. He volunteered the information that, for "perhaps longer than a week," he had had to roll over on his side to sit up. The history further revealed that he had experienced previous episodes yearly for about 3 years. All of them had lasted from a few days to 3 weeks and had occurred about the same time of the year, the most severe being 2 years before, when he was unable to hold his head upright. The last previous episode had been in October, 1953, when the weakness was primarily in the hands. At this time, a physician gave him "injections," with gradual recovery over a few weeks' time. At no time had there been any dysphagia, loss of sphincter control, diplopia or respiratory difficulty. There was a history of polydipsia and polyuria of several months' duration. The past history and review of the systems were noncontributory except that the patient's mother had had diabetes and had died at the age of 70.

Physical examination revealed a well developed, well nourished man who was slow in speech as well as motions. The gait was apparently normal except that he was unable to walk either on his heels or on his toes and could walk a straight line only with great difficulty. The Romberg sign was absent. He was unable to sit up from a supine position without turning on his side and using both arms. There was mild winging of both scapulas, the left being greater than the right. There were no sensory changes; the tendon reflexes were present and equal bilaterally though somewhat decreased, and there were no pathologic reflexes. Muscle examination failed to show any fasciculations, but there was definite weakness of the left shoulder girdle and both pelvic-girdle muscle groups. The remainder of the examination was negative.

The blood pressure was 142/90. The pulse was 64, and the temperature 97.8°F.

An x-ray film of the chest was interpreted as normal. Routine examination of the urine was negative for albumin and sugar, and microscopical examination of the sediment was negative. Examination of the blood showed a red-cell count of 4,500,000, with a hemoglobin of 14.0 gm. per 100 cc. (90 per cent), and a white-cell count of 8500, with a normal differential. The sedimentation rate was 44 mm. in 1 hour. A serologic test for syphilis was negative.

On the following day the weakness was more pronounced, and the patient was admitted to the Deaconess Hospital for further observation. On January 8 the serum potassium was 2.1 milliequiv., and the sodium 155 milliequiv. per liter, and the calcium 11 mg., and the fasting blood glucose 129 mg. per 100 cc. The blood urea nitrogen, inorganic phosphates, cholesterol and creatinine were all well within normal limits. Another potassium determination on January 9 was 2.25 milliequiv. per liter. An electrocardiogram showed a sinus rhythm at a rate of 60 per minute. The QRS complex measured 0.08 second, and the QT interval 0.44 second, and there was a depression of the ST segments in Leads 1 and V_5, with low to flat T waves in all leads. A test dose of 0.5 cc. and then 1 cc. of 1:1000 solution of neostigmine was given subcutaneously, with no discernible evidence of improvement. On this day the patient was so weak that walking was difficult and carried out only with a slapping, shuffling gait. It was impossible for him to lift his arms but a few inches, and he was able to feed himself only by laying his arms on the table and bringing his mouth down to his fork at the level of his food. The weakness affected the muscles of all extremities but was most severe centrally.

Because of the rapid progression of symptoms over these few days of observation, it was considered mandatory to start treatment promptly. Accordingly, on January 9, oral administration of potassium was started, 4.5 gm. being given daily in 3 divided doses. The response was gratifying, for the day after therapy was begun the patient was able to walk well and to lift his arms over his head, and felt much improved. On the 2d day his strength was apparently

normal to gross testing though even on the 4th day of therapy, January 12, the blood potassium was only 2.7 milliequiv. per liter. An electrocardiogram on this day, however, showed a definite change, with a more normal T wave in all leads, a QT interval of 0.36 second and an isoelectric ST segment. By January 16 the blood potassium had risen to 4.4 milliequiv. per liter.

A glucose tolerance test on the 5th day of therapy, when the serum potassium was still low, revealed a diabetic curve, with a blood sugar of 200 mg. per 100 cc. after 2 hours. A urea clearance test was within normal limits. Several attempts were made to reproduce the symptoms by use of a low-potassium diet, high-glucose intake and insulin subcutaneously. However, these were unsuccessful, and the patient was discharged from the hospital on January 16.

Since discharge from the hospital he has received no supplemental potassium therapy by mouth and, in spite of this, has had no recurrence of his symptoms. The polyuria and polydipsia have not recurred. The blood potassium on January 27 was 5.2 milliequiv. per liter, and the sedimentation rate was 15 mm. in 1 hour. An electrocardiogram on this date showed even further reversion toward normal (Fig. 1). On March 3 the serum potassium was 5.17 milliequiv. per liter and another glucose tolerance test showed a more normal curve (Fig. 2). When last seen on July 1, the patient was still carrying on normal activity without a recurrence of symptoms.

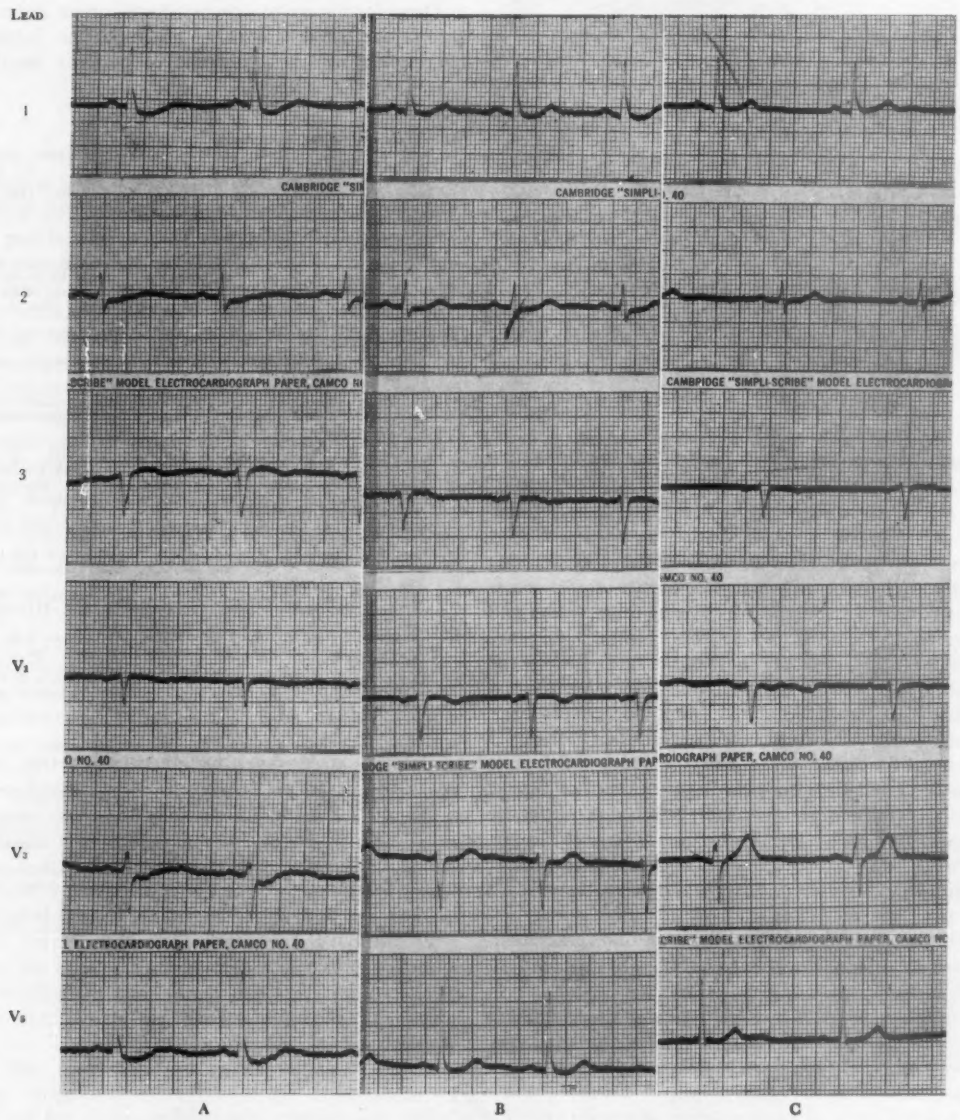

FIGURE 1. *Electrocardiograms Taken during the Acute Attack of Periodic Paralysis on January 8, 1954* (A), *When the Serum Potassium Level was 2.25 Milliequiv. per Liter, on the Fourth Day of Therapy* (B) *and after Complete Recovery* (C), *When the Serum Potassium Level Was 5.20 Milliequiv. per Liter.*

Summary and Conclusions

The case reported above fulfills the criteria for the diagnosis of sporadic (periodic) paralysis. The existence of hypopotassemia and related electrocardiographic changes during the acute attack is pointed out.

Several other interesting features are significant enough for further emphasis: the age (fifty-five years) is relatively late for first onset of symptoms; the gradual onset and cessation of symptoms, sometimes covering an interval of two or three weeks and never having culminated in complete paralysis, are unusual; the blood sedimentation rate during the acute attack was 44 mm. in one hour (Westergren method), as compared with 15 mm. three weeks later, after complete recovery; the symptoms of polydipsia and polyuria before and during the acute attack have been described by others (in the case reported above, these symptoms were completely relieved by adequate therapy and cessation of the attack); and, to my knowledge, a prior report of an abnormal glucose tolerance test in the syndrome of periodic paralysis has not been made.

The fact that the interval between onset and cessation of symptoms was prolonged made it possible to perform a glucose tolerance test on the fifth day of therapy, when the serum potassium level was still relatively low; the curve was abnormal but reverted to normal two months later.

These facts seem to support the theory of abnormal carbohydrate metabolism as an important factor in the etiology of the syndrome of periodic paralysis.

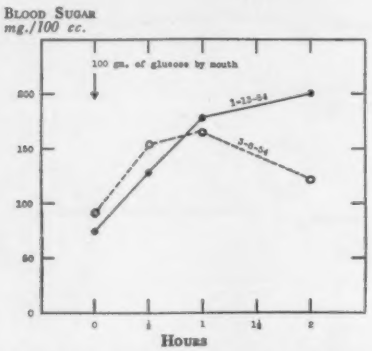

Figure 2. *Comparison of the Glucose Tolerance Test on the Fifth Day of Therapy, When the Serum Potassium Level Was Still Low, with That on March 8, When the Level Was Well within Normal Limits (5.17 Milliequiv. per Liter).*

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SPECIAL ARTICLE

PATHOGENESIS OF READING DISABILITY

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MOST physicians, whatever their specialty, now accept mind, body and social behavior as continuous and profoundly related expressions of the entire person. Who is to say whether Johnny is fat hipped because he needs pituitary or because he cannot read? Whether he hits other children because he is jealous of his new baby sister, or because he is too fat? Whether he cannot read because of lack of love, or lack of oxygen? He is a bundle of cause and effect, each treading on the other's heels. Twenty-four hours a day, with unpredictable immediacy, he is reacting to internal and external pressures.

The medical and social scientists keep working for predictability. They know little enough why people fall ill and get well or why they succeed or why they fail. To narrow the field to a recent area of study, investigation and attempted cure and prevention, just what is known about why some children can "read" — the quotation marks are used advisedly — and why some cannot?

As diabetes indicates a maladjustment in the body's balance, a "specific reading disability" points toward failure to make certain adjustments society requires of a successful personality. Yet, according to estimates now available, perhaps 12 to 15 per cent of boys and half that number of girls show symptoms of this deviation from society's norm. A specific reading disability consists of such a complex set of phenomena that its intricacies can probably be best appreciated by a glance, first, at some of its symptoms.

What does the grade teacher see? The child reverses letters within words: *kitchen* for *chicken, untied* for *united.* One student wrote that his father was working for the *Untied Nations;* another, about ten years of age, wrote that his father was an *unclear physicist.* The child reverses sequences, reading perhaps *May of first* for *first of May.* His eyes deliver absurd anagrams to his mind. He reads *show* for *slow, hot* for *shot, up* for *down, civilian* for *soldier.* And if he does see *soldier,* he may both read and spell it *solider* or *shoulder.*

His speech may follow an analogous pattern. He can say *Silver War* for *Civil War, subsiding* for *presiding, Consution* for *Constitution, bastik* for *basket.* Or he has his moments of baby talk: *wiffeh* for *river, pity* for *pretty, Massusetts* for *Massachusetts.*

In addition, his spelling is often highly specialized, to say nothing of individualized. A bright, charming, athletic boy of eighteen once wrote the following mournful end to a theme about an early morning crow-shooting expedition.

> The brids singe in the tress. At a sigmal [signal] the moth [mother] bird flies up and disappears into the sunrise. The air is fresh and clean and virgin. Tub [but] the mate of the mother is not so luck [lucky]. With a deautiful [beautiful], bitiful [pitiful] milddle [melody] in his throat, he dies from the balst [blast] of our gun. The crow lies in a demoralizing blooby [bloody] mess.

The teacher also observes certain behavior patterns. The young person hates to read; he panics in a test; he may stammer or send up other signals of tension like knee jerking, nail biting, paper tearing, face fussing, hair pulling (both his own and that of other students). If he is one kind of person, he tells the world of his frustration in unacceptable language. He may steal, cheat, destroy property and bully. If he is another kind, he becomes a hobby boy, captain of the basketball team, skilled in shop and, on rare occasions, unusually popular with the girls.

In general, then, the teacher, unless he is too busy or too obtuse, sees a student who is suffering from a sort of foreign body in his organism known as words. He suffers when faced with words he has to write, words he has to say, words he has to read. His handwriting tends to be cramped, illegible and immature. His spelling, as demonstrated above, is often something for the Smithsonian Institution. His oral reading may end in a choked silence, in utterly irrelevant confabulation or, more dramatically, in vomiting, even in fainting, as happened to one student when she was asked to read aloud in the third grade. Silent reading is slow, incorrect and obviously distasteful and almost painful.

What does the parent complain of? Bobby never reads — seems to prefer radio, shop, baseball, ornithology, telephone conversations or even helping his mother with the dishes. He simply will not write letters. He is "stubborn." He will not try. Perhaps he is stupid. If he were only like his older sister who is the parents' pride and joy! She is always on the honor roll. Bobby plays with children much younger than he. He seems to enjoy the company of the maid, the handy man and the not-so-nice children down the block.

By adolescence, Bobby's deviation has perhaps taken a more dynamic turn: he breaks things, takes

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things, raids the icebox all day long, becomes ill at examination time and hectors his siblings unmercifully. Or he may spend hours in his room, the shades down, day dreaming or sleeping. He seems to be often ill, with asthma, hives, colds, generalized fatigue and allergies. It may be significant to note here[1] that Dr. William Kottmeyer, in charge of the reading program in the St. Louis public schools, found from a study of 924 children in the St. Louis language-arts centers that physical handicaps were more frequent among the children who had had difficulty with reading than among a group of children selected at random. A similar study, with similar results, is reported by Eames.[2]

And what are some of the doctor's observations? Bitten nails, perhaps a facial tic, extreme fatness or perhaps hollow-eyed undergrowth or awkward overgrowth. There may be some metabolic disturbance and a history of eye strain, headaches or unexplained nausea. That now famous bump on the head when Sonny was small may turn up in the case history, too. In addition, prematurity, left-handedness or ambidexterity and certain suspected birth injuries sometimes constitute part of the case history. "Johnny never talked until he was four." "Jane couldn't walk steadily until the age of six." "Walter still sucks his thumb and he is thirteen."

On the other hand the patient is sometimes a picture of eupeptic well-being and social charm. His almost certain anxiety and discouragement run as Alph, the sacred river, ran, "Through caverns measureless to man Down to a sunless sea."

The psychiatrist who must try to measure those caverns may spot other stigmas of the disabled reader. Buried underneath the extreme good manners is hostility. Thinly underlying the surface of jocular smoothness is a deep substratum of self-flagellation and generalized depression. The patient tends to make only a thin and scattered identification with the parent of the same sex. The girls are often horse loving, pants wearing, crop haired and unfeminine. The boys may be passive, indecisive, very polite and dependent on their mothers; although often attractive, they are unable to make a satisfactory relation with girls even on the coke-and-movie level. They have given up trying to compete or to identify themselves with their fathers. They are often the forgotten generation with the absent father: absent at war, absent at making a great professional success or even absent at philandering. Sons of doctors, who are necessarily absent while giving their time and their best attention to other people's children, are conspicuous among this forgotten generation, as may be the sons of any unusually successful, unusually distinguished, unusually bright and sensitive fathers. The sons learned long ago that they could not win with such spectacular fathers. The race went to the swift, and the battle to the strong; they are neither so swift nor so strong as their fathers are.

If the psychiatrist has made use of the skill of a clinical psychologist to administer and interpret projective tests, he will have found out that these disabled readers, more often than not, cannot foresee themselves as any kind of whole adult. They envisage no future, no success, no pattern. They do not project themselves as citizens, as earners, as spouses or as parents. For them there is only an insulated bit of time and a temporary island of personality: me and now.[3,4]

Finally, the psychiatrist especially sensitive to language significances may note certain occasions for baby talk, mispronunciations and slips of the tongue. He will sense the singsong voice and the awkward and circuitous locutions. A recent example is offered by a college freshman who, when asked to interpret the proverb, "Smooth Seas Make Poor Sailors," wrote, "No experience makes an inefficient person to life and its holes." The psychiatrist and others notice the monotonous vocabulary. When asked to interpret "Dig a Well Before You are Thirsty," another student wrote, "If you know you are going to need a thing then you should get other things ready so that when you need the thing you can have it."

Sometimes a quite original private vocabulary blossoms, however — a direct descendant of Mrs. Malaprop. A sixteen-year-old girl, telling of an incident in a restaurant said, "Those kakters bobbled in and slooped down in a chair. They were fudged in between the wall and the counter. And I was simply befuddled when they spoke so rudely to me." And it will be helpful here to give, again verbatim, some definitions of a highly intelligent seventeen-year-old boy:

Ossify: this means to astonish, to frighten to death.
Palpable: good to the taste, good to eat.
Pander: that means run fast, panting down the track, thundering down, you know, pander, pander, pander, that's the way it sounds.
Pariah: that's the black pariah, the wagon that takes away the drunks.
Platitude: that's how high aviators get into the air.
Aptitude: that is the feelings you have about something. Your father says: I don't like your aptitude toward using the car.
Brandish: that is what you have in restaurants sometimes, brandish cherries. They burn with ice cream.
Henchmen: those are the guys that sit on the bench I suppose, the ones the coach never uses.
Flagrant: that is the way flowers smell, or a field of daisies.

As reading specialists who have had the opportunity to test and to work with a good many hundred disabled readers of all ages, we have come to certain tentative conclusions about how they feel and why they feel that way.

In the first place, there seems to be a deep-seated, pervasive, terrifying kind of disunity in the world of the disabled reader. He reveals this in a dozen unmistakable ways. While reading aloud he stops dead in the middle of a word, or of a sentence, ignoring all punctuation, so that form falls apart and he is left with only the scattered remnants of an idea. He

may even tear a word limb from limb, laboriously spelling it out. For example, he looks at "thought," makes seven senseless sounds, t, h, o, u, g, h, t, as he "reads" it, and finds himself clutching at seven fragments instead of one whole idea.

His spelling, too, shows these symptoms of fragmentation. Syllables are omitted or inserted, and affixes added or subtracted in a fine frenzy of piecemeal anxiety. As he writes, he sounds out each letter as if, quite unrelated to other letters, it led a life of its own. Even his pencil leads this nightmare independent existence. As his mind intends to write *big*, his hand, with the most maddening perversity, writes *gib*. He looks at this irrational product of disunity between hand and mind and begins to feel like an accident going somewhere to happen. By now he hardly dares to look any word or idea in the face, so hagridden is he with the dismembered ghosts of ideas.

Why is he seeing the world unsteadily and seeing it in pieces? Why is his ability to communicate— read, write, speak, think — in a fragmented condition? The whole answer, if it were known, would be a complicated matter. A part of the answer may be that this young person tends to be emotionally immature and knows it; his schoolmates also know it. This immaturity completes the vicious circle around which he is hopelessly treading instead of progressing in a steady direction of learning, of growing and of gaining mastery over his environment and over himself. If immaturity means self-absorption, unrelatedness to the group and lack of self-discipline, is this not simply a redefinition of what the student does with words?

In the second place, the disabled reader feels inadequate, inferior and chronically alarmed. "I'm the rotten egg of my family," says a beautiful nineteen-year-old girl as she enters the office for a test. "You'll stop working with me when you discover that I've got rocks in my head," remarks a fifteen-year-old boy (I.Q., 135). "My father's a bank president and a Brain. My mother's a Phi Bete from Wellesley. My brother's a Summa Cum Something from Harvard. I'm the only one they are all ashamed of." "When a test is coming up everything inside me freezes. My hands, my memory, my brains. I want to go to the bathroom and to lose my lunch all at the same time."

They feel inadequate because, measured against their culture's demands, they are inadequate. Society requires that at a given age they learn to read, and keep on reading. They have been unable to meet that demand. The ignorance of parents and teachers about the real causes of their "laziness," their "stubbornness" and their "stupidity" has led to tragic, if unintentional, mistakes. Adults have bribed, scolded, compared, deplored and mocked — all in vain.

The causes of their inadequacy are many and various; neurologic, sociologic and emotional, among others. Hinshelwood,[5] an English ophthalmologist, as early as 1900, came to the conclusion that this difficulty might arise from defective development of the part of the brain that registers visual memories. Later, Orton,[6,7] believing that the term congenital word blindness was inaccurate, suggested the word strephosymbolia — twisted symbols — as a better description:

> . . . At the third or associative level, however, destruction of one hemisphere may result in complete loss of the associative function, resulting in inability to read (acquired word blindness), while destruction of exactly the same area in the opposite hemisphere will not give rise to any symptoms whatever. That hemisphere in which destruction produces loss of the associative function is called the dominant hemisphere, and may be either the left or the right, according to the side which habitually initiates the motor responses of the individual. . . it is obvious that the visual records of one side only are used in symbolic association and those of the other are elided or inactive in this process. . . If, however, the physiologic habit of complete elision of these engrams of the nondominant hemisphere were not established, their persistence might readily serve to explain the failure to differentiate between p and q and between was and saw, and also to account for facility in mirror reading and mirror writing . . . Thus would be explained those confusions of direction which have been extensively recorded in the literature and which as here described seemed to characterize all the cases of my own series.

Because the left-handed or, indeed, the left-eyed person may tend to perceive words from right to left instead of from left to right, he can find himself reversing or misplacing letters, reversing word sequences and, as already pointed out, even reversing meaning. If he is in enough of a panic, he goes farther—he confabulates or invents totally irrelevant words or even sentences.

Thus, when a child with neurologic confusions and indecisions is faced with having to see from left to right, he may be overcome. A book perceived from any direction is still a book. But a word, in Western culture, must be read from left to right: *tops* is *tops*, not *spot*. A sentence must be read from left to right, or as has been seen, *gib*, not *big*, and *guns*, not *snug*, turn up on the page to frighten the child and to mystify the parent.

Disagreement with Orton's explanation of causes has been advanced by eminent reading specialists, among whom is Gates.[8]

> Left-handedness, left-eyedness, and mixed eye and hand dominance are possible but doubtful, at most, slightly influential factors . . . The idea that confused brain dominance or lack of dominance should be the cause of such reading difficulties was considered too speculative to be serviceable.

The neurologic factors may not, or may, as Orton[6,7] suggests, be the beginning of the child's problems. But they are by no means the end. By the close of the first grade, the emotional reactions to reading difficulties have set in. To understand these, one must look honestly at certain sociologic pressures in contemporary civilization.

In the first place parents have been impatiently awaiting the day when they could answer the puzzling and often embarrassing question of Junior by saying: "Here is a book. Read it. It will tell you."

Next, parents, relatives, neighbors and playmates have been concentrating with varying degrees of jealousy, complacency or emulation on the Great Divide when Johnny is no longer a baby, but can "read." Ability to read marks his entry into the charged field of the knowledge of Good and Evil. It will also, fortunately, keep him quiet on rainy days. One should not forget the symbolic significance of the ability to "read." Its acquisition is almost like a puberty rite. After it, parents know that Johnny is "all right." The more he reads, the more normal he is assumed to be.

Thirdly, there is the pressure of entering school at a standard age — despite the fact that boys tend to mature more slowly than girls. Right here may be the first stumbling block for small boys. They are not so ready to read as their sisters. In addition, sociologic pressures have already started. Girls stay in the house, playing verbal games like dolls, house, cooking and dressmaking. Girls usually have their mothers at home to verbalize with, to imitate and to identify themselves with. Wordwise, at six or seven, they are already ahead of their brothers.

The boys, on the other hand, under a different set of mores pressures, have been absorbed in the more or less wordless pursuits of gang warfare (with a vocabulary limited to "dit-dit-dit-you're dead"), animal watching, baseball, machine watching and assembling and disassembling objects. The boys have begun their career of being the Strong and Silent Sex. They are not verbalizing; they are doing.

Another possible reason that small boys find greater difficulty than girls in learning the communication skill may be the reverse of their sisters' good fortune. All day long a girl can see her mother being a woman. She knows what she is and what she is going to grow up to be. But, early in the morning, the boy's father disappears in a car or into a subway. He returns, tired, not with a wheelbarrow full of potatoes or with a flock of sheep, but with a brief case stuffed with papers. This is temporarily discarded in favor of a newspaper, Martinis or a dull "grownup" talk with the mother or guests. How is the boy to know what a man does, what he is, what being a man means, or what his function in the family really is?

In early years one probably learns by identification. How much harder, then, for the boy with an absentee mysteriously-occupied father to learn, than for the girl who helps her mother shop, watches her grow a baby inside her, sees her cook and even shares in her troubles! Reading, which means learning and prepares one for becoming an adult, seems much less rewarding to the boy than it does to the girl. Why bother to work on growing up, to become like this phantom who scuttles into a hole in the ground in the morning and returns at night with nothing more tangible than a brief case?

We should go no farther in searching for the causal factors of reading difficulties without calling attention to the deeply thoughtful and articulate work of Perry and Whitlock, both of the Bureau of Study Counsel at Harvard.[9-11]

Still another hypothesis for the cause of reading disability is that it may have been unconsciously laid down long before reading begins. The child, whose first comprehension of spoken admonitions from parents was both vague and unwilling, has perhaps nourished this vagueness as his best protection against growing up. He has developed psychic deafness. Unable adequately to internalize the precepts of his parents at the appropriate time in his growth, he identified himself with his parents either incompletely, or not at all. If they were resentful or loveless toward him — and many parents are toward their children — he did not want to be like them, or even to hear them. He finally came, in truth, not to grasp the meaning of their spoken word or any directive word.

As a young person works at growing himself up, understanding transmutes itself into doing. If a child does not hear — and hence does not comprehend — the communications of an adult whom he does not wish to emulate, he is, in his own scale of values, exonerated from the burden of introjecting such advices and culture pointers into his inward set of moral standards. Ignorance of the law is a perfectly wonderful excuse — to avoid being like those unloving adults.

At this point it is suggested that, among the weaknesses observed in adults' reading, the inability to understand directions ranks high. Perhaps any directions, from how to make lemon jelly to how to assemble a prefabricated house, smack of the early yea's and nay's. One may carry resentment against authority up to the directions on the label of a bottle. And one may carry it into a full-fledged "reading disability."

Conclusions

Before six the child learned, or failed to learn, by hearing. At about seven he began to learn, or not to learn, by reading. The child who has determined to have no truck with grownups and their stern world may protect himself from understanding the written word by a "disability" as he has already protected himself from understanding the spoken word by a psychic deafness. Any year, even up to the age of sixty, he may turn up in a reading clinic. Even if he limped somehow through college, his disability undiagnosed, he may continue all his life to avoid books, to "read too slowly," to "concentrate poorly" and to "fear he may miss something," with the result that he does a superb job of self-sabotage. He reads so slowly that he misses almost everything.

Thus, at the end of the first grade, his slowness and "stubbornness" and his preference for outdoor games and hobbies have already frustrated the child's teacher, who, by the way, happens to be a woman.

Without intending to, she may have praised the glibber readers and publicly deplored the boy, or even humiliated him. His emotional problems connected with what may presently turn into a full-fledged reading disability have begun. These feelings of inadequacy and almost unbearable frustration — for if the child has a specific disability, without expert help he will see the wrong word some of the time no matter how hard he tries — then begin to create a climate of generalized discouragement. More and more tasks seem to be too hard. Fewer goals, especially those aiming toward adulthood, seem attainable. The conviction that he cannot win may strike at the very core of the child's security and at his certainty of his parent's love. Rightly or wrongly, he has come to equate good reading, school success and high marks with parental approval and love. If he disappoints his parents by being "slow" or "stupid" they might no longer love him. Then he is lost indeed.

This deep fear probably has lifelong significance. It may be one of the main causes of the adult reading problems, of which there are legion. The adult who "can't concentrate," who must look at every word or who proudly announces that he is a perfectionist may be reliving the experience of his own childhood when he matched good reading with good love. Now his anxiety for approval has been transferred to the boss or to society. He may even be indulging in that form of sibling rivalry known as healthy business competition. As one spectacularly successful businessman of thirty-six, in one of our reading courses remarked, "I have gotten where I am because I just don't make mistakes. I can hardly risk making them now by trying to read faster." Thus, if the adult fails to grasp every bit of meaning (much of it quite useless to his purposes), he may forfeit the approval he so covets. Hence, he must gaze at each word, look back at material he already knows, point with his pencil, say the words aloud or subarticulate, just as he did when, at six or seven, he was learning to read. By this ritual magic he can surely catch and keep the acceptance, love and success essential to his welfare. This is the essence of the whole problem of "perfectionism." Who tends to expect too much of himself? Is it not the child or the adult who is afraid that if his performance is less than A+ he will be cast into the outer darkness? This fear is, of course, described by its victims in worthy terms: ambition, idealism, high standards, devotion to job and so forth.

Moving a step farther, the perfectionist may even stop trying altogether, lest, if the results of his effort were less than perfect, he might give a tangible and irrefutable demonstration of his unworthiness. Hence, at adolescence, the child who is so polite, who does not dare to guess, who has not the courage to try, who parrots separate words instead of relating whole ideas and who "never makes any trouble" for teacher or parent. He finally never makes any trouble or anything else for that matter. And hence, among adults, the unfinished theses, the unanswered letters, the unwritten articles, the unpainted pictures, the unplayed sonatas and the unread books.

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MEDICAL PROGRESS

CLINICAL PULMONARY PHYSIOLOGY (Continued)

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Ventilation and Gas Exchange at Rest

The *tidal volume* is the amount of air moved through mouth and nose with each breath. *Minute ventilation* is obtained by addition of all tidal volumes exchanged during one minute. The easily measured minute ventilation is not an informative expression of the quantity of air available to the alveolar surface for gas exchange. With each inspiration the dead-space air within the respiratory passages must be flushed into the lungs before ambient air can reach the breathing space. This dead-space volume, usually 100 to 150 cc.,[103] must be subtracted from the tidal volume before effective air exchange, or *alveolar*

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ventilation, can be calculated. When breathing is rapid and shallow, minute ventilation at the mouth may appear adequate, but tidal excursions may not be much larger than the dead-space volume so that little gas exchange takes place.

Respiratory Dead Space

Accurate calculation of alveolar ventilation requires knowledge of the dead-space volume. The respiratory system is composed of *conducting airways* (the mouth, nose, pharynx, larynx, trachea, bronchi and bronchioles) and the *exchange airways* where rapid gas exchange takes place (the alveoli, alveolar sacs and atria). Owing to diffusion and anatomic deformation during respiratory movements no sharp boundary exists between the gas that has been exposed to the exchange airways and the dead-space air. The *physiologic dead space* is now defined as the volume of the conducting airways down to the place at which large changes in gas composition occur.[103] The expired gas consists of two components, one from the dead space and one from the alveoli. The volume of the physiologic dead space can be calculated, according to Bohr,[104] from the easily determined volume and concentration of a given gas in the expired air, from the concentration of the same gas in the alveolar air and from the concentration of the gas in the dead space, which is the same as that in the inspired air. The problem is thus the measurement of the alveolar concentration of the gas.

"Alveolar air" was first obtained by forcible expiration through a long tube and by removal of the last portion of air from the tube. This so-called Haldane–Priestley[105] sample is no longer considered representative of alveolar gas because the interruption of normal breathing causes an alteration of the alveolar respiratory quotient.[106] A more adequate sample of alveolar gas can be obtained by continuous sampling of the last portion of each breath.[106-109] If carbon dioxide is used as the gas for calculation, according to Bohr, the pressure in the arterial blood can be substituted for the alveolar pressure of the gas on the probably correct assumption that the two tensions are virtually the same.[110] More recently Fowler[103] has used nitrogen for this calculation. The concentration of the expired gas is measured by a physical method[111] and is recorded continuously after an inspiration of pure oxygen. By this technic the physiologic dead space averaged 156 cc. for males and 104 cc. for females. It could be shown that the dead space is not a constant entity; it increases during voluntary hyperventilation and exercise, a 3000-cc. increment of the gas volume in the lungs causing a rise of about 100 cc. in the dead space. The physiologic dead space does not change with age and apparently is only slightly larger in the presence of emphysema.[112]

These newer methods may eventually be adapted for clinical use. However, the measured dead-space volume cannot be evaluated with certainty until the composition of alveolar gas and its relation to ventilation and perfusion are more clearly defined.[3]

Minute Oxygen Consumption

This is a function of metabolism and is never decreased by a degree of cardiopulmonary disease compatible with life. On the contrary, in certain situations when the work of breathing is increased the oxygen requirement may be larger than normal.[49,113] For respiratory studies the importance of the postabsorptive state has been overemphasized. In over 200 normal subjects and patients with cardiopulmonary disease, the metabolic rate after a recent meal was rarely more than 5 per cent above the predicted level if fifteen to thirty minutes of rest was allowed before examination.[52,54,88] Basal oxygen uptake is closely related to body surface area and diminishes with age; the prediction formulas of DuBois and DuBois[114] and Aub and DuBois[115] are still widely used. For various age groups the oxygen consumption averages from 126 to 146 cc. per minute per square meter of body surface.[2]

Oxygen Debt Demonstrated by Oxygen Breathing

Certain patients with cardiopulmonary disease show a temporary increase of oxygen uptake on changing from room air to oxygen breathing.[116] The additional oxygen take-up, or "oxygen debt," has been considered a measure of arterial-blood unsaturation during room-air breathing. The volume of the oxygen debt[91,116,117] and more recently the time required for complete saturation of the arterial blood,[118-120] determined by oximetry, have been used as indexes of cardiopulmonary insufficiency. However, the correlation between the size of oxygen debt and the severity of disease is poor.[25] Much of this work was refuted when it was shown that no quantitative or qualitative relation exists between oxygen debt and measured arterial oxygen unsaturation.[121] For over-all evaluation of pulmonary function these tests are inadequate. The measurement depends on too many variables; the rate of arterial oxygen saturation increase is influenced by minute ventilation, dead space, inflation of the lung (functional residual capacity), effectiveness and uniformity of intrapulmonary distribution of gases, alveolocapillary diffusion, the magnitude of arteriovenous shunts, and circulation time and, in addition, is affected by the variables of all ear-lobe oximetric measurements.[122] Oxygen debt on breathing of oxygen, which does not occur in normal persons, is often confused with oxygen debt accumulated during exercise, a normal phenomenon.

Ventilation Equivalent for Oxygen and Rate of Oxygen Removal

The "efficiency" of ventilation has been expressed by relating the volume of ventilation to the volume of oxygen taken up. Two expressions for this "oxygen

absorbing power"[123] are in common use. The ventilation equivalent for oxygen is the number of liters of ventilation required for an oxygen uptake of 100 cc.[124] It ranges from 2.2 to 2.8 liters per 100 cc. and, as with other data based on resting ventilation, variation is great and the borderline between normal persons and the severely ill is blurred.[125,126]

The other expression, the rate of oxygen removal, is the number of cubic centimeters of oxygen consumed per liter of ventilation.[127] Varying normally between 38 and 48 cc. of oxygen per liter of ventilation,[2] this rate, with appropriate change of the decimal point, is the reciprocal of the ventilation equivalent. The usefulness of these ratios is small, first, because they are subject to all the vagaries of minute ventilation measurements at rest and, secondly, because they are based on minute rather than alveolar ventilation.

In my experience an abnormally high ventilation equivalent (or low ratio of oxygen removal) can be attributed most often to hyperventilation due to apprehension and attention to breathing.[10,82,88] The ventilation equivalent for carbon dioxide is not affected by short periods of "voluntary" overbreathing because carbon dioxide elimination increases in proportion to ventilation.[9,128,129] Because of the great diffusibility of carbon dioxide this ratio is not comparable to the ventilation equivalent for oxygen.

The second limitation — that these ratios are based on volume exchange at the mouth rather than on alveolar ventilation — also leads to much misinterpretation. If minute ventilation and oxygen uptake are the same in a patient with rapid, shallow breathing and in another with slow, deep respirations the ventilation equivalent for oxygen is the same in both. However, in the second case alveolar ventilation is greater and the ventilation equivalent, purporting to express "efficiency," actually should be larger in terms of oxygen uptake and in terms of air made available to the exchange surface of the lungs.

Evaluation of ventilation equivalents requires analysis of *hyperventilation* and its many ramifications. Again, alveolar ventilation should be the basis of observations. Clinically, hyperventilation is difficult to assess. With rapid shallow respirations or with dyspnea there may appear to be excessive breathing but less air may in fact be exchanged than the occasion demands. This is strikingly noted in chronic cardiac failure in which the "hyperventilation" often described cannot be confirmed by objective laboratory measurements.[88,130]

Matheson and Gray[131] recently proposed a classification of hyperventilation based on the ventilation equivalent for oxygen. Excessive breathing, which is due to an increased oxygen requirement of the tissues, is called *metabolic hyperpnea:* during exercise or with hyperthyroidism or fever the ventilation equivalent is normal because ventilation and oxygen uptake are increased equally. Excessive breathing without a correspondingly larger oxygen uptake is termed *compensatory hyperpnea* and is characterized by an elevated ventilatory equivalent (or a reduced ratio of oxygen removal). However, the factors that control ventilation are so numerous that the single finding of compensatory hyperpnea cannot localize abnormalities of the respiratory or circulatory systems. The thesis of multiplicity of respiratory stimuli of Henderson,[132] brought up to date by Gray,[133] suggests that stimuli leading to compensatory hyperpnea may be mediated reflexly or chemically or may originate within the central nervous system. Conscious or subconscious psychic influences or any of a number of local defects of the cardiopulmonary system may be involved. Diminished alveolar ventilation due to rapid, shallow breathing, inefficient or uneven distribution of gases, abnormal structure of the pulmonary parenchyma with altered stretch reflexes, thickened alveolar-capillary membranes leading to defective diffusion, ineffective transport of oxygenated blood, metabolic acidosis and many other factors may be responsible for compensatory hyperpnea. Additional information is required for interpretation of an abnormal ventilation equivalent and for evaluation of the "efficiency" of ventilation.

Exercise Tests

The limitations of evaluation of the cardiorespiratory system at rest have been emphasized. In all but the most severely disabled a stress must be applied to obtain physiologic measurements differing significantly from the normal, to elicit subjective complaints of fatigue and dyspnea and to evaluate disability. Certain tests of lung volume and breathing capacity require maximal effort, but the stress involves the respiratory system only; observation of this system's ultimate function of providing tissue gas exchange is not possible.

A large variety of exercise tests have been devised to suit the work to the type and severity of the disease and to satisfy multiple and often mutually exclusive experimental requirements.

A type of work that is *familiar to most patients* is desirable because dyspnea and fatigue are then indicative of limitation of customary activity; the necessity for prolonged training and variables due to differing efficiency are eliminated.[134,135] Walking at a given rate on a level course[85] and climbing stairs or steps meet this requirement.[2,125,136-138] Treadmill walking[138-140] and riding on a stationary bicycle ergometer[22,141] require some practice. Bicycle motion in the supine position[142] and turning a hand crank[21] are worst in this regard.

A mild stress that can be tolerated by sick patients and can be applied without fear of aggravating pulmonary tuberculosis is often desirable. The step tests[2,137] and the standard walking exercise[85] were designed with these considerations in mind. However, the limitations of resting studies also apply to

some extent to mild exercise. The slight effort preoccupies the subject insufficiently to prevent voluntary alteration of breathing and taxes only the severely disabled. With the walking test, hyperventilation cannot always be demonstrated when other tests show defective gaseous distribution or diffusion.[79,83,143]

The *severest exercise* that can be tolerated may be of interest in the study of pulmonary disease[127,140,144]; increasing stress can be applied by a treadmill with variable incline[140] or speed.[139] Latent cardiorespiratory insufficiency can be demonstrated by this technic, and voluntary or subconscious hyperventilation does not enter as a disturbing factor. Maximal oxygen uptake has been considered most significant,[140] and the severity of the tolerated stress itself is an indication of the extent of disability and has been used for a performance index.[139] Whether maximal *intensity* or maximal *endurance* of work are being tested depends on the severity of the stress.[145] Of the three factors involved in capacity for severe work, the neuromuscular and the psychologic (motivation) are more important in determining maximal intensity because the third, the cardiorespiratory factor, does not "catch up" until some time after the exercise has been completed. Therefore, tests of maximal working capacity are more suitable for evaluation of the organism as a whole.

Three different phases of exercise — the *anaerobic period,* the *steady state* and the *recovery period* — have been distinguished. The last two have been of interest in clinical evaluation of pulmonary function.

During the first, or *anaerobic, phase,* which lasts thirty to forty-five seconds, up to three times as much work can be performed as can be accounted for by maximal performance of heart and lungs.[134,146]

Usually, gaseous equilibrium is re-established between alveoli, blood and tissues after a few minutes of steady, moderate exercise; under certain circumstances up to an hour may be required[147] before this second phase, the *steady state,* is reached, when aerobic and anaerobic processes are balanced, the body "pays as it goes" and no further oxygen debt is incurred. During exercise severe enough to require more than 2 liters of oxygen per minute, a steady state cannot be maintained.[134] Studies during the steady state have received increasing attention because certain newly developed technics of cardiopulmonary evaluation can be interpreted only under this condition. Simple treadmills are well suited for application of prolonged moderate exercise and for concomitant studies requiring stationary equipment.[8,138] Steady exercise in the supine position is possible with foot-pedal arrangements and metronome timing or ergometer observation.[142]

The duration of the third, or *recovery, period* depends on the intensity and duration of the work,[134,148] on age, on previous training[149,150] and, to a lesser extent, on the severity of cardiac[125,127,148,151] or pulmonary disease.[125,152,153] Interest in this last period was stimulated when it was found that more oxygen is used by the tissues than is supplied during exercise.[134] The larger than basal oxygen uptake, which persists for some time after the exertion, has been named *exercise oxygen debt.* It is a cumulative index for the sum of nonoxidized metabolites stored during the adaptation phase of the work; it is usually expressed as percentage increase of oxygen uptake during early recovery compared to basal oxygen uptake.[125] In normal subjects after standard exercise 15 to 74 per cent more oxygen is consumed during the first five minutes of recovery than during an equal period under basal conditions.

The exercise oxygen debt as a test of cardiopulmonary function has enjoyed much undeserved popularity. The percentage expression is unfortunate because oxygen debt is an amount and not a rate: oxygen uptake during recovery depends not only on the volume of the oxygen debt but also on the rate of decrease of oxygen consumption.[145] Actually, in very sick patients, the oxygen uptake after exercise may remain elevated for a long period but at a rather low level. Under these circumstances measurements during the first five minutes suggest an erroneously low oxygen debt. Furthermore, the term "oxygen debt" for increased metabolic rate is not appropriate because the uptake is related to intensity and duration of exercise and not to basal metabolic rate. The determination of oxygen debt is fraught with technical difficulties because the advocated spirometric technic does not permit differentiation of changes in oxygen uptake and alterations in the functional residual capacity.[27,125,153,154] Because of these definitive and technical difficulties and because of the variables introduced by training and intensity of exercise, the range of oxygen debt between normal subjects and patients with serious pulmonary disease overlaps considerably[152]; the test does not differentiate cardiac and pulmonary disease as was once thought, and the oxygen debt may be elevated or normal in either condition.[134,148-153]

Standardization of exercise is a frequent requirement. This may have two meanings: a known quantity of work (load) expressed in ergs, joules, calories, kilogram meters or foot pounds per unit of time or watts, and a work of undefined magnitude but standardized so that an identical effort can be imposed on different patients or, at least, on the same patient on repeated occasions.

Knipping's[144] handcrank ergometer, the Krogh[22] bicycle and modifications are "standard" exercises of the first type. More elaborate machines have been designed for patients who cannot work at a fixed rate in which the resistance increases as the subject works more slowly so that the same work is produced irrespective of the speed.[155] Aside from the technical difficulties of calibrating the resistance, inertia and efficiency of the mechanical unit, quantitation of the

work expenditure of the subject and standardization in this sense may not be appropriate. The ergometer indicates only the amount of external work, ignoring the work of moving the limbs against gravity, which may equal or exceed the amount of work required to actuate the ergometer.[156] Variation in the length and weight of the extremities causes different leverage factors, and no absolute relation exists between the work output of the machine and work performed by the patient's musculature.

Mechanical efficiency, calculated by relating the energy expenditure of the patient (caloric requirement during the work minus basal caloric requirement) to the external work indicated by the ergometer,[141,157] should be viewed with equal skepticism. Many extraneous factors, unrelated to the severity of the disease, affect this calculation. The caloric requirement varies with training[134-136,158] and with the number and efficiency of the muscles used.[159,160] The energy requirement of the patient rises with increasing speed even if the work load remains the same.[134,-145,161,162] This is attributed to the greater work required at faster speeds in overcoming frictional and elastic resistances offered by muscles, joints and fascial planes. Finally, difficulties arise in establishing the basal oxygen uptake because of the stimulating effect by exercise on basal metabolism, which may last for many hours and is unrelated to duration and intensity of the work.[163] In general, expressions of work in terms of physical units and in terms of efficiency are misleading.

No attempt is usually made to quantitate the work during treadmill, stair and walking exercises. It is accepted that heavier subjects work harder than slight patients, and the factor of height and weight is minimized by calculation of ventilation or oxygen uptake in terms of body surface.[2,10]

Breathing Reserve and Dyspnea Index

Ventilatory insufficiency may be due to a reduced ventilatory capacity, an increased ventilatory requirement or both. The *breathing reserve*, which is the maximal breathing capacity less the minute ventilation,[164] correlates these two factors. It is often expressed as percentage of the maximal breathing capacity:

$$\frac{MBC - MV}{MBC} \times 100.$$

In normal subjects at rest, the breathing reserve is 88 to 95 per cent of the maximal breathing capacity and decreases somewhat with age.[2,131] Dyspnea usually becomes apparent when the breathing reserve is reduced below 70 per cent.[2] Without exercise the usefulness of the expression is limited. With a normal maximal breathing capacity a twofold increase of resting ventilation reduces the breathing reserve only 3 to 6 per cent.

The *dyspnea index* is the reciprocal of the breathing reserve or the percentage of the maximal breathing capacity required for a given exercise.[85,140] The harder the work, the larger the numerator, and the greater the likelihood that hyperventilation will be reflected by an elevated dyspnea index. During a standard walking exercise, dyspnea hardly ever occurs if the minute ventilation is less than 35 per cent of the maximal breathing capacity, and dyspnea is always present if it is more than 50 per cent.[85] This *walking index* and similar calculations are used for evaluation before thoracic surgery.[165-167]

Calculations of breathing reserve or dyspnea index add little to information obtained from the maximal breathing capacity alone unless the exercise is severe.[6] My experience with the standard walking exercise in more than 3000 patients indicates that there is a better statistical correlation between shortness of breath and dyspnea indexes predicted according to body surface than those based on actual performance.[10] During this mild exercise, the maximal breathing capacity is the dominant factor.

Breathing Pattern

There has been much comment concerning variation in the appearance of the spirogram among apparently normal persons.[59] *Breathing patterns* have been analyzed for the study of personality defects, cardiovascular neuroses and psychoses.[168-170] Sighs and swallows, variations in depth and rate of breathing, respiratory pauses, inversion of patterns and periodic changes in the midposition have all been related to emotional disturbances. Although certain real respiratory symptoms such as dyspnea and tetany can be attributed to neuroses, detailed analysis of breathing patterns is not ordinarily within the scope of cardiopulmonary-function studies. For differentiation of the hyperventilation syndrome and malingering from cardiovascular disorders the appearance of the spirogram is so important as to merit familiarity with this type of analysis. The literature on this subject has been reviewed by Caughey.[171]

Pneumotachography

All conventional spirographic methods are beset by two difficulties: resistance breathing and recording of volume rather than rate of air flow.

Obstruction to breathing cannot be eliminated even if large-bore tubing, low-resistance valves and circulating fans are used.[24] At rest and during mild exercise the effect of the resistance offered by well constructed respiratory apparatus is negligible. The usual consequences of obstruction such as alteration in rate and depth of breathing,[18,24,49,50,80] hypercapnia, hypoxemia and increases in oxygen uptake and functional residual capacity are immeasurably small under these circumstances. However, the breathing pattern, being sensitive to slightest obstruction, is definitely altered by spirometry at rest — minor irregularities, slight delays and small out-of-phase air movements are dampened out by the resistance and inertia

of conventional apparatus. Furthermore, patients with partial paralysis of the respiratory musculature or with a disorganized respiratory center cannot be observed by conventional spirometry because the small added resistance and dead space are not well tolerated. Finally, for studies during severe exercise, for determination of the maximal breathing capacity and particularly for measurements of the frictional resistance offered by lung tissue and airways, the resistance offered by the usual instruments becomes a hindering factor.

The pneumotachograph permits registration of the breathing patterns without introduction of measurable inertia and offers a resistance that is approximately a hundredth of that encountered in conventional spirometry. More important, the pneumotachogram curve represents instantaneous *rates of flow* whereas the exchanged *volume* (the usual spirogram) is expressed by the area under the curves. Mathematically, the pneumotachogram at any point stands for the slope of the spirogram at that point (first-order differential), and a spirogram can be obtained from the pneumotachogram by mechanical[172] or electric integration.[173]

The instrument is based on the fact that the rate of flow through a tube is proportional to the resistance (pressure drop) provided that streamlined flow is maintained.[17] Originally, a bundle of capillary tubes was used to maintain laminar flow and to offer the necessary minute resistance.[174] Recently, the use of fine-mesh wire screens with cone-shaped approaches as "prime movers"[175,176] and the introduction of aluminum membranes as pressure-sensitive devices have brought this method closer to clinical application. Translation of the "pressure drop" into electric energy by pressure-sensitive vacuum tubes,[177] electric condenser methods[178] or linear differential transformers[173] has permitted simultaneous recording of many of the physical events of respiration.

Pneumotachography is applicable in patients with poliomyelitis, myasthenia gravis and other neuromuscular disorders who do not tolerate ordinary spirometry. It is most useful in studies requiring simultaneous recording of rate-of-flow, volume, intrapleural pressure,[172] intraesophageal pressure[178] or expired-air composition.[103] Pneumotachography is valuable in the study of breathing patterns[49,179,180]; nomenclatures for various points of the curves have been suggested,[180,181] but it appears that the normal respiratory pattern is so variable that detailed description of minor changes will never assume clinical importance.

Mechanics of Respiration

Analysis of the mechanics of breathing requires knowledge of the anatomy of the structures involved and an understanding of the stress-strain relations of the respiratory pump and lungs. The relative neglect of the engineering aspects of respiration by clinicians and physiologists has been attributed to their traditional preference for chemistry over physics as an investigative tool.[182]

Rohrer et al.[183] were the first to present a detailed analysis of the over-all mechanical behavior of the respiratory system. They pointed out that the *elastic forces* acting on the lung and surrounding structures depend on the degree of deformation and are therefore a function of *volume* whereas the forces resulting from *friction* due to both gas-flow and lung-tissue resistance are related to change of volume or *rate of gas flow*. Three variables must be measured to analyze the mechanical properties of the lungs and respiratory tract separately from the surrounding structures: the pressure applied to the system, which is the pressure difference between the airway opening (mouth) and the surface of the lungs (pleural pressure); the volume of gas displaced; and the rate of volume displacement.[179] The total force required to move a given volume of gas at a given rate must overcome elastic recoil and tissue as well as airway resistance. Elastic recoil alone can be measured between phases of the respiratory cycle when there is no flow and hence no forces are active to overcome resistance. Once the total force and the elastic behavior have been defined the frictional resistance behavior can be calculated by simple subtraction.[173] The mechanical difficulties and clinical dangers of intrapleural measurements and the laborious graphic separation of the elastic from the nonelastic forces have limited application of this method in the past to occasional determinations on normal subjects and a few patients with emphysema and congestive heart failure.[172,184-186] Several recent developments in instrumentation have brought this type of analysis closer to clinical application. The demonstration that intraesophageal pressure changes closely mirror intrapleural changes has eliminated the need for thoracentesis.[173,187,188] The cathode-ray oscilloscope is used for direct plotting of pressure-flow curves,[170,189] and electric subtraction of elastic from nonelastic forces facilitates resistance measurements without tabulation and replotting of simultaneously obtained graphic records.[99,173] Electronic integration of the rate-of-flow curve permits direct recording of volume without planimetry.[24,173] Studies of elastic forces can be simplified further by brief external airway interruption to achieve static conditions without the co-operation of the patient.[99,190]

The ease with which the lung is deformed (the elastic property) has been expressed in terms of *compliance* as volume change per unit of pressure change.[173] More normal subjects of different ages and of both sexes must be studied, and certain technical variables must be eliminated before compliance can be fully evaluated. A correlation between certain lung volumes and compliance has been demonstrated in normal persons.[191,192] Clinical application of these methods has resulted in interesting findings, particularly that of a relatively normal compliance in pulmonary emphysema[99,190] with marked decrease

during rapid breathing. This has been held as objective evidence of "air trapping" and uneven pulmonary ventilation. A reduction of compliance proportionate to the reduction in the total lung capacity has been found in poliomyelitis,[193,194] and a reduced compliance in asymptomatic patients with mitral stenosis with no abnormality of pulmonary function demonstrable by more conventional methods of examination.[195,196]

Of even greater interest is the measurement of *total pulmonary resistance*. In pulmonary emphysema this factor, expressed in terms of pressure change per unit of rate of flow, was five times larger than normal during quiet breathing and twenty to one hundred and fifty times larger than normal during maximal effort.[99] Interestingly enough, resistance was increased by breathing with a voluntarily deflated chest and decreased during respiration at the maximal inspiratory position.[173,200] The total pulmonary resistance is composed of *resistance to air flow* through the bronchopulmonary passages and the *frictional resistance of the pulmonary tissues* to deformation. A number of efforts to separate these two components have centered on measurements of the first of the two factors, the airway resistance. The "alveolar"-mouth pressure difference has been recorded during very short instants of airway interruption.[172,180,197,198] Recently, it has become apparent that this method does not eliminate the tissue resistance element.[199] Foreign-gas studies are based on the premise that breathing of a gas with a density and viscosity different from that of air should lead to a change in airway resistance but will not affect tissue resistance.[17] Preliminary work with argon-oxygen mixtures suggested that the tissue friction factor is negligible both in health and in emphysema.[200] The over-all breathing resistance is considerably decreased by breathing of helium-oxygen mixtures.[198] More detailed studies with helium and ethane have shown that about a third of the total is due to tissue resistance, and Rohrer's assumption of streamlined flow in the airways, merely interrupted by eddying at points of changing diameter, has been disproved.[201]

The net result of the opposing elastic forces exerted by the lung and the surrounding structures can be analyzed for any given volume of gas within the system. This type of study has led to the development of the *pressure-volume diagram* of the thorax and lungs. Elaboration of this early concept[202-204] by Rahn et al.,[80] Fenn[182] and Otis, Fenn and Rahn[205] has contributed much to the understanding of respiratory physiology. The magnitude of the subdivisions of the lung volume, the end-expiratory position of the chest, the vital capacity and its changes with body position and pressure breathing and the work of breathing have been interpreted in terms of this pressure-volume pattern of the thorax and lungs.[48,49,182] Abnormal findings in various pulmonary diseases, predicted on the basis of this pattern, have coincided with results of conventional volume measurements. Clinical considerations of positive pressure and resistance breathing have been clarified.[49,206] Because these studies of the total respiratory system include the respiratory musculature, the elastic forces exerted by the lung alone cannot be isolated. Construction of the pressure-volume relation under passive conditions (the "relaxation pressure curve") requires elimination of respiratory muscular activity[80,182] or the use of a body respirator.[202,203,205] Manual methods of artificial respiration have been evaluated by this method in trained men, but clinical application of this analysis is obviously not possible. The collected studies from the laboratory of Fenn, Otis and Rahn[206] concerning the chemistry and mechanics of pulmonary ventilation include several of the most important contributions to clinical physiology during recent years.

(To be concluded)

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MEDICAL INTELLIGENCE

CHLORPROMAZINE TREATMENT FOR RELIEF OF ITCHING IN SEVERE REFRACTORY NEURODERMATITIS*

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CHLORPROMAZINE,§ a relatively new drug, has already found a wide variety of applications as noted in this journal. Among these are management of manic states,[1] control of nausea[2] and induction of hypothermia.[3]

Pellerat[4] reports its use in neurodermatitis, eczema and other skin conditions. Delay, Deniker and Tardieu[5] state that a case of pruritus was helped by the drug. Per contra, Winkelman[6] mentions urticaria as an occasional complication of chlorpromazine. Bower[7] found 2 cases of dermatitis with redness, scaling and itching of the chest or arms in his psychiatric cases.

Dermatologic applications reported to date appear to be limited to the French literature. Since results published in French journals reach the United States largely by osmosis, a description of the use of the drug in 3 long-standing cases of neurodermatitis may be of interest. These cases were unusually refractory. One of the patients had threatened suicide if relief was not forthcoming. The following case presented an equally difficult problem.

CASE REPORT

A 46-year-old woman was admitted to the Baker Memorial Hospital on February 4, 1954, because of pruritus and dermatitis of 3 months' duration. Four months previously x-ray therapy had been given for metastasis of a breast carcinoma to the right side of the neck. Three or 4 weeks later radiodermatitis of the overlying skin developed that persisted and subsequently became localized neurodermatitis. This continued with partial remissions and acute exacerbations, including exfoliation and generalized eruption at intervals. Before admission there was no response to calamine lotion, vaseline, Burrow's solution and colloidial baths. There was only a partial temporary response to cortisone, applied locally or administered internally. She became quite dependent on meperidine (Demerol) hydrochloride for relief of itching and "nerves."

The past history included a simple excision of the left breast for carcinoma 9 years previously. Because of local recurrence radical mastectomy was performed 3 years later Metastases, which were treated with x-rays, appeared 2 years before the present illness. There was no previous history of skin disease or of any nervous disorder.

Physical examination revealed a well developed and well nourished woman with a surgical scar due to removal of the left breast. There was a lichenified dermatitis with excoriations on the anterior part of the neck and chest. The cubital folds showed tiny areas of lichenified dermatitis. The rest of the body had infrequent excoriated papules.

Examination of the urine was negative. The hemoglobin was 13.4 gm. per 100 cc., and the white count 12,800, with 81 per cent neutrophils. The eosinophil count was 29 per cubic millimeter. The bilirubin was 0.2 mg. per 100 cc. Cephalin flocculation was ++ at 24 and 48 hours.

On psychiatric evaluation the patient appeared incessantly active; some part of her body was continually in motion. The skin was constantly being rubbed, poked, patted, slapped or picked at. There were bouts of scratching of almost frenzied intensity that left her skin raw and bleeding. Her speech was rambling, repetitive and incessant. The mood was labile: there were moderate irritability, occasional facetiousness and a few brief intervals of depression. She complained of exhaustion, but was unable to sleep. Psychomotor activity strongly resembled that found in classic hypomanic states, although euphoria and play on words were both absent.

Management during 5 weeks in the hospital included bed rest, sedation and topical applications, with only meager, transient relief of symptoms.

At this time our attention was called to the effectiveness of chlorpromazine in the management of hypomanic conditions. It seemed indicated to control restlessness and scratching. The intramuscular route was selected and continued for 1 week. The dose was 50 mg. 3 times a day. Later, the drug was given by mouth, 50 mg. 4 times a day. Precautions for parenteral use were observed as described by Bower.[7]

Within 24 hours the itching became less severe; restlessness and overactivity were diminished. With the absence of pruritus and cessation of the compulsive desire to scratch there was a prompt disappearance of excoriation, scaling and lichenification. The patient improved so rapidly that she was able to go home within 10 days, at which time she was being maintained on oral administration of the drug.

Her skin continued to do well in spite of the fact that further painful skeletal metastases were discovered on the date of discharge. She was free of dermatitis 2 months after discharge.

DISCUSSION

Encouraged by the response in this case we decided to try chlorpromazine on other patients with recalcitrant neurodermatitis. The first of these was a sixty-year-old man with a history of severe, chronic dermatitis of twenty-four years' duration. He had been seen by many dermatologists. The resident's admission note mentioned "incredibly long" treatment "starting with soaks and salves . . . suffered removal of all his teeth, his tonsils, gall bladder and appendix, without relief. . . . various elimination diets . . . two years in an out-of-state hospital . . . two more years in a different hospital . . . remained in various hospitals continually" for another seven years. A prescribed "trip to Arizona made his condition worse . . . . For the last two years he has noted slight improvement but still itches fiercely."

Currently, he had been receiving massive doses of cortisone, to which he was no longer responding. Chlorpromazine was started intramuscularly. That night he slept for twelve hours, although one of his most distressing symptoms had been insomnia. Since then, his generalized neurodermatitis has gradually improved. While in the hospital, phlebothrombosis developed, requiring surgical attention. Although the postoperative convalescence was difficult his skin has continued to look better.

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§Kindly supplied by Smith, Kline and French Laboratories as Thorazine.

A third patient was then selected. This sixty-six-year-old woman originally had stasis dermatitis of more than ten years' duration that had responded to the usual therapy of bed rest and subsequent surgery. Dermatitis of the face and upper extremities subsequently developed and was thought at one time to be either contact dermatitis or lymphoma.

An acute exacerbation marked by severe pruritus and excoriations required admission to the hospital. The diagnosis on admission was neurodermatitis. She did not respond to conservative therapy. When chlorpromazine was started she experienced subjective relief within three hours.

The last 2 patients are still under observation and are currently receiving hospital care.

No controls have been used in these preliminary cases because the possibility of a relapse presented too serious a risk. Clinically, the improvement noted to date in 3 acutely ill patients has been gratifying.

Several physiologic actions of chlorpromazine seem calculated to be helpful in the treatment of neurodermatitis. These include the reduction of body temperature, which is accompanied by ischemia of the skin and reduced capillary permeability,[8] and the soporific action that tends to promote sleep.

When, as often happens in neurodermatitis, the associated psychiatric condition is vexing, chlorpromazine may be effective in the alleviation of tension states, as well as in the relief of itching. It should be especially helpful when, as in the cases presented above, the intensity of the motor activity verges on the hypomanic.

In severe cases of neurodermatitis chlorpromazine appears to be a timely addition to the therapeutic armamentarium. Further investigation is clearly needed before the drug can be accepted without reservations. The follow-up periods in these cases are not long enough to rule out all possible delayed ill effects, although to date none of those reported in the literature appear to have been serious. Among the undesirable complications described by other writers are painful induration from too rapid injections, postural hypotension and jaundice. Proper precautions should be taken to avoid these and other undesirable side effects.

Summary and Conclusions

Chlorpromazine was helpful in relieving scratching, insomnia and restlessness in 3 cases of severe, intractable neurodermatitis. It seems to merit further trial when hyperactivity and scratching are serious complications and do not respond to other forms of therapy. It seems prudent to emphasize the fact that this is a new drug. Side effects have been reported that may be troublesome. For the present we advise that its use for neurodermatitis be limited to patients who are hospitalized and can be kept under careful supervision.

Follow-up data obtained after this paper was submitted for publication indicate that two points should be emphasized. The first is that chlorpromazine is not a panacea for dermatitis; the cases reported are few in number and others might not respond so well. Secondly, exacerbations of symptoms did occur while the drug was still being administered.

The fact should also be reported that Case 2, supra, died of complications after a thrombosis of the femoral vein. Although autopsy revealed pulmonary edema, bronchopneumonia, arteriosclerosis and nephrosclerosis, the only finding that might be pertinent to the present article was an enlarged liver showing fatty degeneration. Since the patient had not received any of the drug for two weeks before death, it is considered improbable that the liver damage observed was due to chlorpromazine. A more likely cause is malnutrition.

Although reported animal experiments do not indicate any liver damage due to chlorpromazine, clinical studies have revealed jaundice in a small percentage of patients who were receiving the drug. The facts mentioned above suggest that chlorpromazine should not be used indiscriminately. In the cases reported itching, insomnia and restlessness were intractable symptoms, which had become almost intolerable and which were a severe tax on the endurance of the patient. There had been no adequate response to other forms of treatment. At present Case 1 is at home and has been able to discontinue the drug, and her dermatitis has been completely relieved. Case 3 is at home, is receiving the drug in reduced dosage at the outpatient department and is doing well.

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USE OF CHLORPROMAZINE IN THE WITHDRAWAL OF ADDICTING DRUGS*

Preliminary Report

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THE abrupt withdrawal of addicting drugs gives rise to well defined symptoms, including restlessness, nausea, emesis, insomnia and perspiration. Many of these effects, as Himmelsbach[1] has pointed out, are manifestations of disturbances that are autonomic in origin. His findings and those of others[2-4] indicate that the use of opiates, by upsetting homeo-

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§Kindly supplied as Thorazine by Smith, Kline and French Laboratories.

static equilibrium, calls into play autonomic compensatory action, which then becomes a hyper-reaction requiring these drugs to preserve the quasi equilibrium. Consequently, withholding opiates from addicts temporarily produces an autonomic imbalance that results in the manifestations of the abstinence syndrome.

Investigators[5,6] in Europe have reported that a new phenothiazine derivative, chlorpromazine, blocks or appreciably inhibits irritative neuroendocrine reactions. Their findings, therefore, led us to investigate whether chlorpromazine§ would alleviate the symptoms of opiate and barbiturate withdrawal.

TABLE 1. *Clinical Characteristics of 8 Patients Withdrawn from Addicting Drugs with Chlorpromazine.*

PATIENT	SEX	AGE	DRUG	DOSAGE	DURATION OF ADDICTION	COMMENT
		yr.		*mg./day*	*yr.*	
G.K.	M	26	Pentobarbital	900	4	Borderline schizophrenia; insoluble marital troubles.
V.G.	F	34	Demerol	400	2	Functional abdominal pain
K.C.	F	50	Morphine	120	2	Functional abdominal pain
A.S.	M	42	Morphine	90	½	"Renal colic"
A.L.	M	46	Demerol	600	5	Chronic peptic ulcer
C.M.	M	36	Morphine	120	1	Exaggerated complaints from latent duodenal ulcer
M.R.	M	55	Morphine	300	3	Cancer of rectum; perineal resection; colostomy; involutional depression.
R.F.	F	53	Morphine	180	1½	Cancer of breast; radical mastectomy with metastases; fracture of hip.

MATERIAL

The clinical characteristics of 8 patients withdrawn from addicting drugs are presented in Table 1. The patients, 5 men and 3 women, ranged in age from twenty-six to fifty-five years. Five were addicted to morphine, 2 to Demerol, and 1 to pentobarbital. The duration of addiction ranged from six months to five years. Of the 8 patients only 2 had required drugs for control of pain. Five others complained of pain, but physical examination revealed no basis for their complaints. The remaining patient, a barbiturate addict, was a borderline schizophrenic whose marital troubles bothered him considerably. According to Rayport[7] these patients would be classified as medical addicts since they first received the drug from a physician.

REGIMEN

All opiates and barbiturates were abruptly and completely withdrawn, and chlorpromazine therapy instituted. Fve patients were initially given a single 50-mg. dose intravenously and a 100-mg. dose intramuscularly. Four hours later, and every four hours thereafter for the next two or three days, they were maintained on 100-mg. doses, administered intramuscularly. Intravenous infusions of fluids and vitamins were given concurrently. After the third day the patients were placed on oral medication, usually 50 mg. four times daily, and fed a high-calorie diet supplemented with vitamins. Two patients were initially given the drug (100 mg.) intramuscularly instead of intravenously, and continued on this dose every four hours for five days before oral medication, 50 mg. three times daily, was substituted. The barbiturate addict was started on 50 mg. intravenously and 100 mg. orally, and subsequently maintained on oral medication, 50 mg. three times daily.

All patients were followed with liver-function studies — determination of cholesterol esterification, bromsulfalein retention, alkaline phosphatase, thymol turbidity, cephalin flocculation and serum albumin-globulin ratio — before, during and after chlorpromazine therapy. In addition electroencephalographic and electrocardiographic tracings were taken as well as daily intermittent checks on vital signs. When discharged from the hospital, patients were usually maintained on chlorpromazine, 25 to 50 mg. orally three times daily. They were re-examined weekly, and, if necessary, their dosage was adjusted. All continued the therapy for at least a month on an outpatient basis before the drug was discontinued.

RESULTS

None of the patients withdrawn from addicting drugs with chlorpromazine experienced the phenomena that constitute the abstinence syndrome. Most patients, when chlorpromazine was first started, slept for intervals as long as twelve hours, but could be roused by gentle shaking or prodding. All were kept in bed while they were on parenteral medication so that postural hypotension, which sometimes follows the administration of chlorpromazine, would not occur. Seventy-two hours after the withdrawal of the addicting drug the dosage of chlorpromazine was gradually reduced, and oral feedings were started. Unlike the addicts experiencing withdrawal

symptoms, who often have anorexia, these patients ate well. No nausea, vomiting or diarrhea occurred. On a dose of 50 mg., given orally four times daily, most patients were, at first, lethargic and seemingly indifferent to their surroundings. Their attitude might be better characterized as lack of responsiveness because they certainly were aware of what was going on around them. Psychomotor excitement was greatly inhibited. Only the barbiturate addict reported feeling jumpy and gave signs of agitation. Otherwise, no problems of restlessness, agitation or insomnia were encountered. Of particular interest was the fact that none of the patients craved or demanded addicting drugs. As therapy was continued, the psychomotor-sedative effect of chlorpromazine diminished and the patients became moderately alert. In contrast to the restiveness and hostility often seen in addicts during withdrawal, these patients were relaxed, calm and co-operative.

The 4 patients with functional complaints reported relief of their pains, and commented that they felt less tense than usual. It would, of course, be pointless to withdraw narcotics from patients with chronic intractable pain without first relieving their pain. In this series 2 so-called medical addicts were successfully withdrawn from opiates. The first, who suffered from chronic peptic ulcer, remained on chlorpromazine for seven days, being fed parenterally and prepared for surgery. On the eighth day a subtotal gastrectomy was performed, and recovery was uneventful. Postoperatively, he was comfortably maintained on chlorpromazine, 100 mg., given intramuscularly every four hours, in combination with Sodium Amytal, 450 mg. intramuscularly at bedtime, and was discharged twelve days later. The other, a woman with cancer of the breast and widespread bone metastases, was admitted to the hospital because of a pathologic fracture of the hip. Morphine, 30 mg. every hour, failed to relieve the pain. On chlorpromazine she became quiet, and her complaints ceased. After being withdrawn from morphine, this woman has for the past eight months been maintained on chlorpromazine 25 mg., given orally three times daily, and despite the fact that x-ray examinations show that the lesions present before her withdrawal are still present she has required only occasional non-narcotic analgesics for the occasional pains.

Of the 2 remaining patients, both of whom had apparent emotional disturbances, 1 had become addicted while receiving morphine to relieve pain after an abdominoperineal resection, which left him with a colostomy, and the other had become addicted by surreptitiously taking pentobarbital to relieve his tension. The patient with cancer never adjusted himself to the colostomy, became depressed and continually complained of abdominal pain in the region where the incision had been made. Morphine, 30 mg. every two or three hours, failed to relieve the pain. After withdrawal, however, the patient ceased to demand opiates, gained weight, regained his spirits and gradually became adjusted to taking care of himself. The patient who had been addicted to pentobarbital is a borderline schizophrenic with much anxiety and tension that was first related to his being in the service and later to his marital problems. Although his family reports that the patient is improved, his prognosis is doubtful.

Laboratory studies have given no evidence of liver dysfunction or blood dyscrasia in this series. Lethargy, dry mouth and constipation were reported by patients when they took the drug on an outpatient basis.

Since withdrawal plays a relatively minor role in the treatment of addiction, it is recommended that all patients continue to receive psychiatric guidance. Five of the patients in this series have been followed for more than six months, and 3 for three months, and none give any indication that they are presently using addicting drugs.

Discussion

During the withdrawal period addicts treated with chlorpromazine can abruptly and completely discontinue the other drugs with little or no discomfort. This is contrary to the belief that any method of withdrawal that does not use some opiate may result in death of the patient.[7] Restlessness, agitation and insomnia seldom occurred; no nausea, vomiting or diarrhea resulted. Our findings, though preliminary, indicate that chlorpromazine offers many advantages over methadon substitution and morphine withdrawal in the treatment of opiate addicts. Since only one barbiturate addict was observed in this series, no general conclusion can be made regarding the effectiveness of chlorpromazine in managing barbiturate addiction. Results in this patient, however, indicate that the drug is probably of value.

Since chlorpromazine augments the action of narcotics and barbiturates[8,9] it should be used cautiously in persons who are suspected of recently using these agents.

There are several possible reasons why chlorpromazine is effective in managing the opiate-abstinence syndrome. The first, which has already been cited, deals with the findings of French investigators, notably Laborit et al.,[5] that the drug depresses the central and autonomic nervous system. When given in sufficient doses, it has a lobotomylike effect in that patients are relaxed, emotionally indifferent, quiet and immobile. Several investigators[10,11] have reported cure of morphine addiction by prefrontal lobotomy performed to relieve intractable pain. A second possible reason for the usefulness of chlorpromazine in withdrawal of narcotics stems from its potent antiemetic action. Friend and Cummins[12-14] and Moyer and his co-workers[15-17] have reported extensively on this use of the drug. Their results have shown that

chlorpromazine relieves nausea and vomiting caused by morphine, methadon, Demerol and codeine.

The results of this investigation indicate that chlorpromazine warrants further study in the management and treatment of drug addiction.

Summary

A new drug, chlorpromazine, that depresses the autonomic nervous system was evaluated in the treatment of the symptoms of opiate withdrawal, since such symptoms seem related to autonomic hyper-reaction. None of the 8 addicts treated, including 1 barbiturate addict, experienced the phenomena that constitute the abstinence syndrome. They slept most of the time during the first three days of treatment. Afterward, dosage was reduced, and oral feedings begun. No nausea, vomiting or diarrhea was noted. Psychomotor excitement was greatly inhibited. No problems of restlessness, agitation or insomnia occurred, although the barbiturate addict reported feeling irritable. In contrast to the restlessness and hostility often seen in addicts during withdrawal, the patients in this series were relaxed, calm and co-operative. Our findings are believed to indicate that chlorpromazine warrants further study in the treatment of withdrawal symptoms from opiate and barbiturate addiction.

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1. The general bookplate of the Boston Medical Library used for special valuable gifts. Depicting Aesculapius and Hygeia, with the serpent (the caduceus), the lamb, and the flame of life. Artist: L. S. Ipsen, Engraver, S. L. Smith.

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 41061

PRESENTATION OF CASE

First admission. A fifty-two-year-old housewife entered the hospital because of progressive difficulty in walking.

Six years previously the patient first became aware of weakness of the legs, minimal at first but slowly progressive in severity. It became difficult for her to climb stairs, and her legs were becoming more and more tired on walking so that in the three or four months before entry she had given up walking even a few hundred yards. For about a year she had had intermittent pain in the midback and "shooting pains" in the hips, apparently worse with prolonged standing or riding in an automobile. For approximately the same period she had had occasional incontinence of small amounts of urine.

She had otherwise always had excellent general health, except that throughout her life she had had occasional bouts of urinary-tract infection. For about seven years there had been gradual loss of hearing in both ears. Three years before admission she had briefly had episodes of vertigo on rapid turning, and about two months before admission she had an attack of more severe vertigo, with nausea and vomiting, necessitating bed rest for five days. About a year and a half before admission, a urologist found cystoscopic evidence of cystitis, with a patulous left ureteral orifice; on retrograde pyelography, the kidney outlines were indistinct, especially on the left, and there was some deformity of the left renal pelvis. The urinary infection promptly cleared on conservative medical management.

There was no significant family history.

On general physical examination, the patient appeared to be in good health, and there were no abnormal findings. She was right handed.

On neurologic examination, she was alert, intelligent and co-operative. There was no tenderness or deformity of the spine. The cranial nerves were normal, except for bilateral deafness, with preservation of bone conduction. She walked stiffly, on a broad base, staggering to either side with circumduction of the left leg; there were normal swinging movements of the arms. The limbs were of good strength generally on testing, and the posture of the outstretched arms was normal; the grip of the left hand was weaker, and the left arm was slower on rapid alternating movements than the right. Other tests of co-ordination were well performed. Tendon reflexes were very brisk in the arms, the left biceps reflex being slightly more active than the right, and were hyperactive in the legs, more so on the left than on the right, with bilateral ankle clonus. Cutaneous stimuli of all sorts produced active flexion withdrawal of both legs. The abdominal reflexes were absent. The plantar reflexes were strongly extensor bilaterally. Sensory testing showed pain to be intact; cold seemed to be less well felt below the midthighs than elsewhere, but she could distinguish heat from cold; light touch was thought to be impaired over both feet; vibration sense was slightly impaired in both ankles and in the left wrist; position sense was impaired, but not lost in the toes bilaterally. On standing with the feet together, she was much more unsteady with the eyes closed than open.

The temperature was 98.0°F., the pulse 80, and the respirations 20. The blood pressure was 192 systolic, 118 diastolic.

Routine blood and urine examinations were negative, as was a blood Hinton test. Gastric analysis showed the presence of free hydrochloric acid. Roentgenograms of the entire spine were normal except for angulation between the seventh cervical and first thoracic vertebral bodies, and a small spur on the posterior aspect of the sixth cervical vertebra. A lumbar puncture revealed clear colorless cerebrospinal fluid under an initial pressure equivalent to 195 mm. and a final pressure (after 10 cc. had been removed) equivalent to 155 mm. of water. Cerebrospinal-fluid dynamics, including the response to jugular compression, were normal. The fluid contained 12 lymphocytes and 2 larger mononuclear cells per cubic millimeter; the total protein was 133 mg., and the sugar 50 mg. per 100 cc., and the gold-sol curve 5555421-100; the cerebrospinal-fluid Wassermann test was negative. At the conclusion of these studies the patient was discharged on a program of physical therapy.

Second and third admissions (two years later). In the intervening period her condition had remained much the same, except for an increase in urinary frequency and incontinence. Seven months before admission, after a strenuous day, she had a brief attack of "numbness" on the ulnar side of the left hand, associated with difficulty in finding words, and increased weakness of the left leg. In telling of this, she recounted that she had had a previous similar and even

more severe attack about fifteen years previously. She re-entered the hospital for further study.

The general physical examination was negative except for a blood pressure of 180 systolic, 100 diastolic. The heart sounds were of good quality and regular, without murmurs. The neurologic examination was unchanged except that the left leg was somewhat weaker than before and exhibited clumsiness in the heel-to-shin test. The jaw jerk was absent. The deafness had increased; audiograms showed the loss to be most marked for high frequencies.

Routine blood and urine examinations were negative. Roentgenograms of the cervical spine showed no change. Lumbar puncture gave clear colorless cerebrospinal fluid under a pressure equivalent to 190 mm. of water; there was a sluggish response to jugular compression. The fluid contained 8 mononuclear cells per cubic millimeter and a total protein of 133 mg. per 100 cc. and gave a gold-sol curve of 5555555-531 and a negative Wassermann test. The patient was discharged and then readmitted to the hospital three weeks later, when combined lumbar and cisternal puncture was performed. This procedure demonstrated normal cerebrospinal-fluid pressure and dynamics. Both the cisternal and lumbar fluids contained 10 leukocytes per cubic millimeter, several of which were identified as neutrophils; the protein determinations were 103 mg. and 143 mg. per 100 cc. respectively. The gold-sol curve, identical in the two samples, was the same as that previously obtained. On this admission, a strong finger-flexion reflex was found on the right, with none on the left. She was discharged after completion of the cerebrospinal-fluid studies.

Fourth admission (two and a half years later). Her condition gradually became worse until she required two canes for walking, and urinary urgency and incontinence became more severe. She had had no severe or persistent pain.

On examination there was marked spastic weakness of both legs, more severe on the left, but good strength and co-ordination in the arms except for slight terminal tremor on finger-to-nose test on the left. Handwriting was normal. No sensory impairment was found with the usual tests. The other physical and neurologic findings were as before. The blood pressure was 175 systolic, 100 diastolic.

Routine blood determinations were normal. The sedimentation rate was 25 mm. in sixty minutes. The urine had a specific gravity of 1.020 and gave a + test for albumin; the sediment contained white cells and bacteria. A stool examination was negative for parasites and ova. Roentgenograms of the spine showed no change from previous examinations; films of the skull and chest were normal. Lumbar puncture gave clear cerebrospinal fluid with normal pressure and dynamics; the fluid contained 21 white cells, including 3 neutrophils, per cubic millimeter and a total protein of 216 mg. and a sugar of 45 mg. per 100 cc., and gave a gold-sol reaction as before. Measurement disclosed a bladder capacity of about 1000 cc.

The patient received antibacterial treatment for urinary-tract infection, and was discharged after four days in the hospital.

Final admission (ten months later). There was very little change until four days before admission, when the left leg rapidly became very stiff and powerless. On the next day, she noticed some "prickling" in both hands, and later that day the left arm became stiff and useless. Otherwise, there were no new symptoms.

On examination there was severe weakness of the entire left arm and almost complete absence of voluntary movement, with marked spasticity in the left leg. Tendon reflexes were considerably more active in the left limbs than the right, in which the findings were as before. Again, there was no disorder of cranial-nerve function, except for deafness, and no jaw jerk. The only sensory abnormalities were slight impairment of vibratory sense at the ankles and of position sense in the toes. The remainder of the examination was unremarkable. The blood pressure was 145 systolic, 88 diastolic.

Routine blood examination again was negative. The urine contained numerous white cells in the sediment and gave a ++ test for albumin. A tuberculin test was negative in a dilution of 1:1000. On lumbar puncture the cerebrospinal fluid was clear and contained 2 polymorphonuclear leukocytes and 2 lymphocytes per cubic millimeter and a total protein of 138 mg. per 100 cc. and gave a gold-sol reaction of 5555555555 and a negative Wassermann test.

The patient was seen by an ophthalmologist, who found normal disks, moderate retinal arteriosclerosis and normal visual fields. During the hospital stay there was considerable improvement in the strength of the left arm and slight improvement in the left leg. She was discharged after two months.

About three years after leaving the hospital she finally became unable to walk and was confined to a wheelchair. Two years later she was suddenly awakened by an attack of sharp pain in the suboccipital region and was found on examination six hours later to have weakness of the left side of the face and left arm and increased weakness of the left leg. Two hours after that, she became comatose, with periods of Cheyne–Stokes respirations. She remained in this state for about six hours and then gradually recovered consciousness, whereupon she was thought to be aphasic for several hours. During the next four days she improved considerably but was unable to remember any of the events of the first two days of this episode except for a faint recollection of the pain. On examination three months later, she was alert and mentally clear, with no evidence of any speech disorder and no abnormality of the cranial nerves except for deafness. Carotid pulsations were normal. The left arm and leg were extremely feeble, the right leg moderately weak, and the right arm fairly strong.

The intrinsic muscles of the left hand were atrophied. The legs were in a position of extension; the left arm was slightly flexed. Reflexes were as before. The patient reported "numbness" and tingling over the left side of the neck and postauricular region, but there was no sensory impairment to testing in that area. The only other sensory abnormalities were severe reduction of position sense and stereognosis in the left hand and foot.

Four years later, after gradual slight decline, she began to have progressive difficulty in swallowing, for which she was admitted to another hospital. Two days after admission, she became confused and totally unable to swallow. On the following day she went into coma, had a generalized convulsion soon afterward and died three days later — about twenty-two years after the onset of the neurologic illness and sixteen years after the first hospital admission.

Differential Diagnosis

Dr. C. Miller Fisher*: In summary, a woman at about the age of forty-six began to have progressive spastic paraplegia and after fourteen years evidence of involvement above the foramen magnum, either in the brain stem or at a higher level, developed. The great length of the clinical course is remarkable. If one first thinks of the early part of the course characterized by spastic paraplegia several conditions come to mind, which can perhaps be disposed of in order. First of all one could think of spinal-cord tumor, either intramedullary or extramedullary. It is known that some slowly growing gliomas can extend over great lengths of the cord and even into the brain stem without leading to signs and symptoms in proportion to their great extent. I think we cannot expect an intramedullary tumor to be present for more than twenty years, however, and if we can believe the patient's statement during one admission, she had had similar symptoms fifteen years previously — that is, at the age of thirty-seven — so that possibly this disease could have been present for thirty years. An extramedullary tumor, such as a meningioma, can be extremely slow growing as can a neurofibroma, but again a tumor growing in the confines of the spine or posterior fossa for twenty or thirty years that did not lead to more sensory signs or cerebellar signs and cranial-nerve deficit would be most unusual. In addition I think we can accept the information indicating that there was no spinal-fluid blockage although on one test there was some suggestion of block. A tumor compressing the cord should produce blockage of spinal-fluid flow quite early, particularly with increased protein and abnormal cells in the cerebrospinal fluid. Without discussing these two further I think I can go on to other possibilities.

In the early stages of the illness one might have thought of a centrally protruding cervical disk, but when the disease extended above the foramen magnum such a diagnosis became untenable. Also, that condition cannot alter the cerebrospinal fluid in this way, and it is likely to produce a block early.

Another possibility is a bony abnormality of the atlanto-occipital region — an atlanto-occipital fusion or abnormal odontoid process, pressing backward into the medulla. I think I must accept x-ray films of the skull and cervical spine as excluding this diagnosis.

It was noted that there were 10 to 15 white cells per cubic millimeter in the cerebrospinal fluid, and the protein was regularly raised above 100 mg. per 100 cc.; therefore, although the cells were scanty, one must think of inflammation. There is a tendency to regard up to 10 cells per cubic millimeter in the cerebrospinal fluid as normal, but I believe as a rule one does not find more than 1 cell normally. The first infection that comes to mind is neurosyphilis. However, the cerebrospinal-fluid Wassermann test and blood Hinton tests were negative. Because there was no evidence of tabes and the patient probably received penicillin at some time in the course of her illness, I think I can dispose of neurosyphilis.

It would be most unusual for tuberculous meningitis, although it can occur in a so-called en-plaque form, to have a course of twenty or thirty years. So far as I know there were no cultures of the cerebrospinal fluid. One would expect the sugar to have been decreased — and 45 mg. per 100 cc. is a bit lower than usual. Although tuberculous meningitis cannot be absolutely excluded, the course would have been most unusual. If the tuberculous process had been extradural it might have extended slowly, but again thirty years is too long; moreover, one would expect cranial-nerve signs once the lesion extended above the foramen magnum.

Perhaps I should say a word about fungous disease. It was noted that parasites and ova were sought; whether that is significant or not I cannot say. Torulosis has been reported to grow in the meninges for ten to fifteen years. Blastomycosis can take a chronic form, as can coccidioidomycosis, but certainly such a prolonged course would be most unusual, to say nothing of the remarkable sparing of the cerebellum.

Subacute combined degeneration I do not have to consider because this usually starts with numbness in all four extremities and has prominent sensory signs. Also, there was free hydrochloric acid in the stomach juices. Primary lateral sclerosis, if there is such an entity, need not be considered although the limbs were chiefly spastic and sensory abnormalities were minimal. Any sensory change must exclude primary lateral sclerosis. Syringomyelia can extend over great lengths of spinal cord and into the bulb for many years. It can produce changes in the spinal fluid, with cells and increased protein, and there is usually no blockage on lumbar puncture. But I think it is asking too much to say that syringomyelia could involve the motor tracts in this fashion without producing widespread sensory changes; particularly,

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one would expect nystagmus or cranial-nerve signs when the bulb became involved.

Adhesive arachnoiditis, many cases of which have an unknown cause, — or, in other words, are idiopathic, — usually involves the spinal cord first, producing progressive changes. An adhesive process of undetermined nature going on progressively for twenty or thirty years is most atypical. Moreover, there is usually a spinal level on sensory testing, and the arachnoiditis usually does not extend above the foramen magnum. The protein is usually not increased unless there is a spinal block. I think, therefore, that I can dispose of idiopathic adhesive arachnoiditis.

This is a long way of saying that I do not know what this patient had, but there are still a few other conditions to consider, the first of which is multiple sclerosis. Multiple sclerosis can start after the age of forty and run a progressive course, with periods of transient worsening. I have seen a case in which there was no evidence of involvement of the cerebellum and the mind remained very clear until the last. In elderly patients with multiple sclerosis it is said that sensory symptoms are few and that motor-tract signs such as spasticity are more prominent, as in the case under discussion. Moreover, multiple sclerosis can produce changes in the cerebrospinal fluid with increased protein and cells and particularly an abnormal colloidal-gold curve. Merritt* says that multiple sclerosis does not produce neutrophils in the cerebrospinal fluid, and this patient clearly did have them. Also, a spinal-fluid protein as high as this is most unusual, but then this is a most unusual case. The episodes of worsening such as this patient exhibited bring up the question of whether her illness represented only one disease — that is, whether what she died from and what caused symptoms in the last six years were part of the original illness or something new. I have concluded that this is all one illness. When she was first seen, the signs were more on the left side. The first transient attack involved the left side, and in addition she could not speak. The next attack also involved the left side, and the third attack again involved the left side, including the face, so that there is evidence that a process was localized rather than hitting in haphazard fashion in the way of multiple sclerosis. That makes me hesitate to diagnose multiple sclerosis. Also, multiple sclerosis is not usually directly responsible for a fatal outcome; pneumonia is usually the last illness. This patient, after difficulty in swallowing developed, became comatose, suggesting that the primary illness caused death directly.

A saccular aneurysm of the vertebral artery can run a prolonged course and compress the upper cervical cord and medulla, but it would be most unusual for it to extend over twenty or thirty years and not produce cerebellar disturbance and cranial-nerve signs. A fusiform basilar aneurysm would not be likely to compress the pons and produce only leg symptoms; I think swallowing and speech are more sensitive than the function of the legs to bilateral lesions of the pons. Angioma or vascular abnormality of the pons and upper cervical cord comes to mind, but it would not run this course without evidence of bleeding with such an intermittent type of history. I believe lumbar punctures were done fairly close to the attacks. Therefore, since there was never any xanthochromia or evidence of bleeding, I think I can exclude that diagnosis.

There are atypical forms of demyelinating disease of the spinal cord and pons that are capable of producing cells, an increased protein and an abnormal colloidal-gold curve in the spinal fluid but I have not heard of so-called subacute myelopathies that caused this picture. By the way, the dizziness and deafness, I think, were due to otosclerosis and had nothing to do with the major part of the picture.

If I must make a diagnosis my first choice is multiple sclerosis or atypical demyelinating disease despite the objections I have just made, and I think I shall rest on that.

DR. AUSTIN L. VICKERY: Dr. Ayer, you saw this patient; have you any remarks?

DR. JAMES B. AYER: I followed her for years, and when she died I did not know the diagnosis. The various consultants made many of the diagnoses that Dr. Fisher considered and, I think, always with a great deal of question. At least two of the spinal-fluid specimens, both from the cistern and lumbar region, that I took myself were slightly xanthochromic, which was not reported. I should like to stress that, in a series of punctures, at least four, over the years, showed a progressive increase in the protein and cells, particularly the polymorphonuclear leukocytes — but never many. The gold-sol curve remained always first zone. Those findings suggested a progressive inflammatory disease over a period of years. That was not brought out clearly in the protocol.

I did not know anything about oriental diseases, and because the patient had lived in Japan I took it up with Dr. George C. Shattuck, who went over the record but I do not think saw the patient. He could think of no oriental disease that fitted this case. It is interesting that the bladder contained 1000 cc., indicating a flaccid paralysis, whereas the legs were highly spastic, which is a little unusual, suggesting that the disease was not limited to the pyramidal tract. Myelography was discussed several times, and each time was thrown out because there was no block on manometric tests and because we feared it would make her worse.

CLINICAL DIAGNOSES

Multiple sclerosis.
Spastic quadriplegia, unknown cause.
Cystitis.
Hypertension.

*Merritt, H. H. Cerebrospinal fluid in multiple sclerosis. *Brain* 57: 56-58, 1934.

Dr. C. Miller Fisher's Diagnosis

?Multiple sclerosis.
?Atypical demyelinating disease.

Anatomical Diagnoses

Meningoencephalomyelitis, diffuse, chronic, of unknown cause, with quadriplegia.
Pyelonephritis, chronic, severe, bilateral with hydroureters.
Cystitis, chronic.
Bronchopneumonia.

Pathological Discussion

Dr. Vickery: The major post-mortem findings were in the central nervous system. The only remarkable feature about the gross autopsy was the genitourinary-system examination. The kidneys were markedly shrunken, being less than half the usual size, with severe chronic pyelonephritis. The cortex and parenchyma in general were scarred down to a mere shell of their normal thickness, and the adjacent perinephric tissue was fibrotic. The ureters were dilated, and the bladder trabeculated. All the urinary-tract structures showed a severe degree of long-standing infection, the sort of changes often seen in paraplegic persons with so-called "cord bladder" and repeated episodes of infection. Besides those findings and bronchopneumonia, the autopsy was generally negative except for the examination of the central nervous system, which Dr. Richardson will describe.

Dr. Edward P. Richardson, Jr.: This is an extremely perplexing case, which, even after a considerable number of microscopical sections have been studied, presents problems that we have been unable to solve. On gross examination the striking finding was that the spinal arachnoid membrane was greatly thickened, so that the dorsal aspect of the spinal cord, particularly in the lower cervical, entire thoracic and upper lumbar regions, was covered with whitish fibrous material that obscured the landmarks of the cord. There were numerous adhesions between the arachnoid and dura. The midthoracic cord was considerably shriveled and shrunken. Scattered about in the cortex of the cerebral hemispheres were many tiny lesions, about 2 mm. in diameter, that suggested small, old infarcts. The arachnoid was thickened over the cerebral hemispheres, cerebellum and base of the brain, but not as extensively as over the cord. Oddly enough the process was not as severe over the sacral cord and cauda equina as it was higher up. Microscopically, there was loss of nerve fibers peripherally all the way around the spinal cord. The lateral corticospinal tracts were involved, somewhat more on the left, and sections from the thoracic and cervical regions showed more degeneration in the fasciculus gracilis bilaterally than elsewhere in the posterior columns. In the thoracic cord the process was considerably more severe than at levels above and below. Within the greatly thickened pia-arachnoid, there were scattered small collections of lymphocytes, with a very few plasma cells. In addition small arteries and arterioles were severely diseased, with intimal hyperplasia in some of the former and fibrosis with extreme narrowing, or even obliteration, of the lumen in the latter. It is to be assumed that the damage to the cord may to a considerable extent have resulted from impairment of the blood supply, because of these vascular changes. The nerve roots and gray matter of the cord were intact.

Another striking abnormality was marked subependymal gliosis in the walls of the ventricular system throughout the brain. In many places the ependymal layer was interrupted, and tiny nodules of astrocytic gliosis projected through the defect into the cavity of the ventricle. This is the "granular ependymitis" that is found with chronic inflammatory disease of the meninges, and is typically seen in neurosyphilis but also in tuberculous meningitis or any other form of meningitis that goes on for weeks or months.

The microscopical appearance of the tiny cerebral lesions was typical of old infarction — months or even years in duration. One such lesion in the medulla involving the right medullary pyramid and some of the tissue near it may well have been responsible for the pronounced left-sided signs in addition to the paraplegia.

We do not know what the cause of this was. It was certainly a chronic meningeal inflammatory process, with the characteristics of a low-grade infectious disease extending over many years. Syphilis, of course, is a possibility, but seems unlikely in view of the repeatedly negative serologic reactions in both blood and spinal fluid at a time when the disease was active. We have been unable to demonstrate any infectious agent.

Dr. Vickery: Apropos of the remarks that all the possibilities of infection were explored and what Dr. Ayer said too, there was a notation in the record that the patient had been on a trip to the Far East, the Philippines and Japan at one time and that the question of schistosomiasis had arisen. I assume that is what Dr. Ayer talked with Dr. Shattuck about. Dr. Kubik, have you any remarks?

Dr. Charles S. Kubik: I agree with Dr. Richardson that it had the appearance of an infectious process. I do not remember any other case of arachnoiditis with such a long history, and yet there is every reason for thinking that the process was active at the time of death, because of both the clinical progression and the presence of lymphocytes and plasma cells in the subarachnoid space and in some of the perivascular spaces. We looked for yeast organisms in the cells and failed to find any. In a case of blastomycotic infection a number of years ago, with a much shorter history, there were changes in the arteries somewhat similar to those in this case. They occur with any long-standing infection of the meninges.

DR. JACOB LERMAN: I should like to ask Dr. Richardson, since the patient had a long-standing pyelonephritis, if this could have been metastatic small embolic abscesses localized in the area of the meninges.

DR. RICHARDSON: There was nothing that suggested a focal process anywhere. This was extremely diffuse at all levels of the nervous system, although it was worse in the thoracic region than elsewhere. The tiny infarcts in the brain appeared to be bland and probably are explicable on the basis of small-vessel occlusions secondary to the original disease. One certainly wonders whether the pyelonephritis played some part and whether possibly a very chronic, low-grade meningitis was set up with organisms originally coming from there that never produced a fulminating meningitis and never responded to any treatment. Our failure to demonstrate any organisms does not eliminate that possibility. However, this case certainly behaved in a manner that is entirely different from bacterial infection of the meninges, in our experience.

DR. WALTER BAUER: Did the patient receive penicillin or other antibiotic treatment at any time?

DR. RICHARDSON: She received antibacterial therapy, — sulfonamides, — but I do not think she received large amounts of penicillin.

DR. FISHER: Was the mind preserved to the end?

DR. AYER: It was; I do not know about the very end but near the end certainly. There was no repetition of speech difficulty or aphasia.

CASE 41062

PRESENTATION OF CASE

A sixty-nine-year-old retired grocer was admitted to the hospital with a diagnosis of marked cardiomegaly and dyspnea.

A year previously the patient noted slight dyspnea on exertion, which gradually progressed until three weeks before admission, when it suddenly became worse; because of weakness and dyspnea he went to bed. His family physician placed him on a course of digitalis. Another physician saw him later and, observing a large heart shadow on an x-ray film of the chest, referred him to this hospital for study.

The patient had never noted ankle swelling, palpitation or paroxysmal nocturnal dyspnea. There was only slight orthopnea. He had never had hemoptysis, though he had a slight morning "cigarette" cough (he smoked half a package a day). Anorexia had been present for the past six months in association with a weight loss of 30 pounds. He had had no chills, fever, sweats or melena.

Physical examination revealed a very thin, wasted man, who was slightly tachypneic though fairly comfortable lying flat in bed. The trachea was in the midline. The neck veins were questionably distended when the patient was raised to 60°. The anteroposterior diameter of the chest was increased, and there was slight dorsal kyphosis. There was a flat percussion note, and diminished tactile and vocal fremitus and diminished breath sounds over the left lower half of the chest and moist rales in the upper portion. The right lung was clear to percussion and auscultation. The area of cardiac dullness was percussed to the anterior axillary line. The apical pulse was visible. The heart sounds were very distant. Abdominal examination was negative. There was a large nonreducible inguinal hernia on the right and a reducible inguinal hernia on the left. No peripheral edema was observed. There was questionable clubbing of the fingers.

The temperature was 99.6°F., the pulse 110, and the respirations 20. The blood pressure was 98 systolic, 60 diastolic, in the left arm and 110 systolic, 60 diastolic, in the right arm, with a paradoxical pulse (pressure of 10 to 18 mm.).

Urinalysis was negative. Examination of the blood revealed a hemoglobin of 9 gm. per 100 cc. and a white-cell count of 30,000, with 85 per cent neutrophils, 7 per cent band forms, 5 per cent myelocytes and 5 per cent monocytes. The nonprotein nitrogen was 50 mg., the total protein 5.4 gm., the albumin 2.9 gm., and the globulin 2.5 gm. per 100 cc. The prothrombin time was 38 per cent. The serum iron was 40 microgm. per 100 cc. (normal, 125-200 microgm.) and the iron-binding capacity was 17 per cent. The stool was guaiac negative. X-ray films (Fig. 1 and 2) of the chest showed an enlarged cardiac shadow, with a cardiothoracic ratio of 21.5:30.5. There was a suggestion of enlargement of the left atrium. The left leaf of the diaphragm was obscured by the cardiac shadow, or possibly by free fluid in the left pleural space, and was not seen. The lung fields were clear, and there was no pulmonary vascular congestion. On fluoroscopy the right border of the heart was well seen and pulsatile, though there were absent pulsations in the left border. The mediastinum shifted to the left with inspiration. An electrocardiogram showed an abnormal tracing with low voltage in all leads and normal T waves. On thoracentesis on the left 1 cc. of green, thick pus was aspirated; the pus was too thick to allow further aspiration. A Wright stain demonstrated many poorly preserved neutrophils, and a gram stain revealed no organisms. At thoracentesis two days later 150 cc. of similar purulent fluid was removed.

During the hospital stay the temperature fluctuated between 99 and 100°F. The patient continued more dyspneic, with occasional paroxysms of coughing. On the seventh hospital day he suddenly became cool, severely dyspneic and cyanotic. There were bubbling rales throughout both lung fields. The heart sounds were barely audible. With the patient reclining at 15° the neck veins were distended about 2.5 cm. above the clavicles. He was given morphine, oxygen, Cedilanid, aminophylline, Mercuhydrin and rotating tourniquets. There was steady improve-

ment, with clearing of the rales, disappearance of cyanosis and flattening of the distention of the neck veins. The blood pressure remained stabile at 120 systolic, 70 diastolic, with no increase of the paradoxical pulse. Seven hours after this episode, the patient again suddenly became dyspneic and cyanotic, with

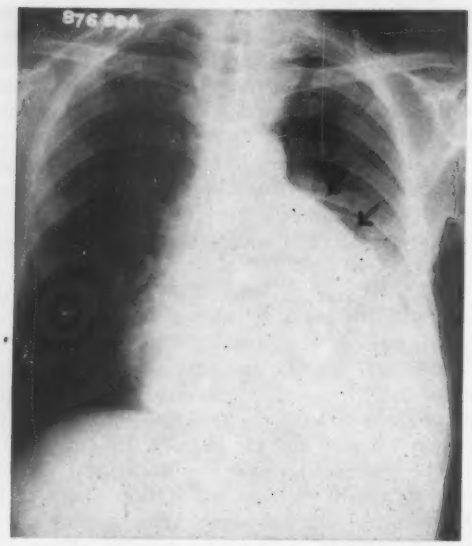

FIGURE 1. *Posteroanterior View of the Chest.*
There is marked widening of the mediastinal shadow, with irregular contour on the left (arrows) and pleural effusion at the left base.

cool extremities and weak pulse, and distention of the neck veins. The blood pressure, always hard to ascertain, now became inaudible. A pericardial needle was introduced transdiaphragmatically, and 600 cc. of green purulent fluid aspirated. At this time no heart beat or respirations were obtained. Cardiac needling failed to elicit a heart beat. He was pronounced dead two hours after the onset of the second episode.

DIFFERENTIAL DIAGNOSIS

DR. JACOB LERMAN*: This patient had vague cardiac symptoms, weakness, anorexia and a weight loss of 30 pounds but no evidence of congestive heart failure initially. On examination there were distended neck veins, an enlarged heart, distant heart sounds, questionable clubbing and signs consistent with fluid in the left pleural space although they could have been due to partial collapse of the left lower lobe from a large heart or pericardium filled with fluid. The slight fever, pulsus paradoxicus and low pulse pressure are suggestive of pericardial effusion. The laboratory data showed leukocytosis and an iron-deficiency anemia, and the x-ray findings again raised the question of fluid in the left side of the chest and pericardium. This suggestion was confirmed by the low voltage in the electrocardiogram. The chest tap revealed fluid, but it is possible that the needle entered the pericardial space. Then there were two episodes of acute pulmonary edema followed by death. I assume that the final tap was in the pericardial space since the needle presumably was inserted in the epigastrium through the diaphragm and must have entered the pericardial space.

May I see the x-ray films, Dr. Hanelin?

DR. JOSEPH HANELIN: What appears to represent the cardiac silhouette is clearly increased in its normal transverse measurement (Fig. 1 and 2). The right margin of the heart is smooth and was observed to pulsate normally at fluoroscopy; the left margin cannot be completely traced, and there is a question whether we are seeing it at all. Among other things one should note the irregular contour of the cardiac silhouette on the left side.

FIGURE 2. *Lateral View of the Chest.*
There is diffuse density of the lower half of the left-lung field that extends for the entire anteroposterior diameter of the thorax.

DR. LERMAN: The left atrium was reported to be enlarged. Can you see that in the view here?

DR. HANELIN: It is difficult to be certain of any chamber enlargement. I am not impressed with the evidence of left atrial enlargement. The esophagus is not displaced as much to the right nor is there any appreciable posterior displacement of the esophagus in the lateral film as one would expect with enlargement of the left atrium. There is an abnormal density in the lower half of the left-lung field that is fairly homogeneous and certainly raises the question of a considerable amount of fluid in the pleural cavity. Unfortunately, I cannot say what is happening to the pulmonary parenchyma in this area. The peculiar density that extends anteriorly in the lateral

*Associate physician, Massachusetts General Hospital.

view probably corresponds with the irregular left mediastinal contour. It is most unusual for such a shadow in this projection to represent the cardiac silhouette. One may wonder about the significance of the inspiratory shift. There are a number of explanations. There may not have been a true inspiratory shift, but a fixation of the heart creating that illusion, resulting from mediastinopericardial chest-wall adhesions. This type of shift could also occur with atelectasis on the left side. I must say that in the film supposedly in inspiration the position of what appears to be the heart is approximately normal. It would have been helpful to see films made in inspiration and in expiration. I cannot tell anything about the status of the left main-stem bronchus. The upper lobe must be fairly well aerated. I am uncertain whether there is some obstruction of the left-lower-lobe bronchus.

DR. FARAHE MALOOF: Is that an abnormal shadow above the aortic knob on the left?

DR. HANELIN: That may be the great vessels.

DR. LERMAN: This is very confusing, and the description by Dr. Hanelin has confused me all the more. So far I think that the evidence points to the presence of pleural effusion. Do you agree?

DR. HANELIN: Yes.

DR. LERMAN: In spite of the fact that this patient did not have pain in the past or a history to suggest the development of pericardial or pleural effusion, the signs point to it. The needle tap showed that the effusion was purulent although no organisms were discovered. How can I put these together? The commonest type of purulent pericardial effusion is that associated with pneumonia, but this patient had no history of pneumonia. There are, of course, many cases of silent pneumonia or walking pneumonia in which empyema and pericardial effusion may develop.

Could it have been tuberculous pericarditis? Most patients with tuberculous pericarditis have advanced pulmonary tuberculosis, which this patient did not have. Consequently, I can discard that diagnosis.

Although the x-ray findings seem clear cut enough for fluid, some of the signs in the lungs are consistent with a collapsed lower lobe produced by pericardial effusion, the so-called Ewart sign — dullness, diminished breath sounds, diminished tactile fremitus and so on. Usually, one hears bronchial breathing over the area of collapsed lung, but none was mentioned, and I assume that the physicians listened for it.

Could the fluid in the chest have originated from below the diaphragm, such as one sees with a ruptured viscus? There was no history for this, so it is only conjecture.

Could the empyema have been associated with a septic embolus? Purulent empyema may occur with a septic embolus, but there was no history for this condition. Consequently, I shall discard it. There was evidence of impairment of liver function — the low total protein, the reversal of the albumin-globulin ratio and the low prothrombin concentration. This can be explained by the long-standing infection, together with the congestion of the liver resulting from cardiac tamponade. The question of atrial enlargement was raised, but Dr. Hanelin will not confirm this so that I shall disregard it as not being significant. I was bothered by the absent pulsation of the left border and normal pulsation on the right. This is consistent with pericardial effusion when one side is more involved than the other so as to obscure the pulsations on that side. Pleural fluid on the left side also could obscure pulsations of the left border of the heart.

I am somewhat surprised that with this much fluid there was no more shift of the mediastinum than was indicated in the lateral projection of the x-ray film, but I suppose that the pericardium could have been held firmly by adhesions, either pleuropericardial or between pericardium and chest wall, to prevent the shift. Dr. Hanelin mentioned the peculiar pulsation that may have been more apparent than real; if it was real it could have been due to adhesions between the pleural surfaces, pericardial surfaces and chest cage so that as the chest cage moved the pericardium moved with it.

The possibility of neoplasm has to be considered. Encapsulated empyema may result from necrosis in rapidly growing tumors of the lung; such a tumor could secondarily involve the pericardium. Except for the suggestion made by Dr. Hanelin of the irregular left surface of the pericardium, there is not much evidence for tumor. Tumor of the pericardium, although a rare disease, is also a possibility; it can become necrotic, break down and produce pericardial effusion. I think that this is a long shot. In favor of pulmonary tumor is the fact that the patient had a long-standing cigarette cough, anorexia and weight loss. Against it is the fact that he had no pain and the absence of a clear-cut x-ray picture of pulmonary involvement by tumor.

The acute pulmonary edema could have been due to increasing tamponade or to a combination of infection and strain of the left ventricle caused by adhesive pericarditis, which was probably present, as well as pleural effusion.

I should like to try to determine the cause of the pleural effusion and the pericardial effusion, but I do not seem to be able to do any more than say that pneumonia or carcinoma of the lung was the underlying cause. I do not know which to choose first; my inclination is to choose tumor although I cannot rule out pneumonia and its complications.

DR. EARLE M. CHAPMAN: I should like to ask Dr. Lerman if he means that a bronchogenic carcinoma had extended through the lung and had involved the pericardium, leading to the purulent material within the pericardium?

DR. LERMAN: I think carcinoma can produce empyema in one of two ways: the initial growth may be rapid, with accompanying necrosis, abscess and

empyema, which may then break through into the pericardium, particularly if it is encapsulated — and this looked encapsulated in the x-ray films; or the tumor can invade the pericardium and then become necrotic. I do not know which mechanism operated here, but both can be involved.

A PHYSICIAN: I wonder if a negative smear for organisms rules out tuberculosis even at this stage.

DR. LERMAN: The ordinary tuberculous effusions are not purulent; they are rather clear exudates. Very seldom in this part of the world do we find organisms in the pericardial fluid to enable us to diagnose tuberculosis. When there is tuberculous empyema and pericarditis, there is also extensive tuberculosis of the lung.

A PHYSICIAN: With constrictive pericarditis there is very little pulmonary tuberculosis.

DR. LERMAN: In adhesive pericarditis there is a short history of pericarditis and pleurisy and little else. There are bands of adhesions between the layers and very little pus. I do not remember seeing a case in which pus was obtained by needle. Can you verify this, Dr. Castleman?

DR. BENJAMIN CASTLEMAN: We have had cases of constrictive pericarditis, with active tuberculosis, with which there was a great deal of purulent material.

DR. JOHN C. DALTON: I saw this patient in consultation and later presented him to Dr. David Littmann at a cardiac conference after the purulent material had been obtained from the pleural cavity. We knew the process was a purulent one. If so, and if it had been inside the pericardium, one would have expected inverted T waves in addition to low voltage; instead the electrocardiogram was normal except for the low voltage. Secondly, there was more empyema than the record indicates. This is shown in the films. Dr. Littmann was impressed with the marked discrepancy in the size of the heart in the posteroanterior view and in the lateral films, and also by the fact that good borders of the heart could be seen on the right side and none on the left. Therefore, he thought that this was not a pericardial effusion, but only a purulent pleural effusion.

CLINICAL DIAGNOSES

Purulent pericarditis, cause unknown.
Cardiac tamponade.
Pleural empyema, left.

DR. JACOB LERMAN'S DIAGNOSES

Carcinoma of lung, with necrosis and empyema.
Purulent pericarditis.
Acute pulmonary edema.

ANATOMICAL DIAGNOSES

Bronchogenic carcinoma, left-lower-lobe bronchus, oat-cell type, with metastases to regional lymph nodes and liver.
Secondary bronchiectasis, with abscess formation, left lower lobe.
Empyema, massive, left, with mediastinal shift to right.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy, when the chest plate was removed, we found in the left pleural cavity an extensive empyema with over 2000 cc. of thick purulent material. The left lower lobe was collapsed because of the fluid, which had pushed the mediastinum over to the right so that the mediastinal structures on the left side at the time of autopsy were only 1 or 2 cm. to the left of the midsternal line. The pericardial sac was normal, without any fluid, and the heart was also normal. The needle that had been inserted through the diaphragm must have entered the empyema cavity, which was in the normal location of the pericardium. The cause of the empyema was found in the left lower lobe, which was covered with fibrin and pus. It was completely collapsed and when sectioned was replaced by purulent bronchiectatic abscessed cavities. This was all produced by an obstructing tumor of the main bronchus of the lobe, with metastases to the regional lymph nodes. The carcinoma was of the oat-cell type, which is the one that occurs almost exclusively in the hilus. Two small metastases were found in the liver.

DR. MALOOF: Can you explain the shadow up above the knob now?

DR. HANELIN: The patient is rotated toward the left; I think that what we are seeing here is the great vessels.

DR. CASTLEMAN: There were no involved lymph nodes up that high.

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THE NONREADER

THE mind of man is untrammeled until it is exposed to education. Relatively speaking, the first six years of life are free years. During this period the child is in most intimate contact with the family and his immediate neighborhood. Whatever his cultural heritage may be, he is given a chance to absorb it. Then a change occurs. The child enters the first grade and thereafter, in the eight years of grade school, he is subjected to a pressure, to a molding process, about as uniform as the rungs on a ladder. First grade, second grade, third grade and so on, the child proceeds, and standards of conformity are rigidly drawn around him. Under the orthodox system he is taught the letters early, tools as old as education. Then he is shown how these letters form simple words. This is called "spelling." Along with spelling he learns to "read." He also learns to recognize sequences of letters formed into words to make sentences. He learns that words represent things: "cat," "rat" and "dog." He learns that some imply action, others position and so forth. Then he proceeds from simple sentences to little stories and so on to longer stories. This process takes years and is essential to all other processes in education. It is called commonly "spelling" and "reading" and, of course, "writing," but all three are essential to what may be called in general "learning."

In brief, the child "learns" in some proportion to the way he can spell, read and write. No one has to date discovered any method of simplifying or eliminating these brief and essential procedures, and there is no indication that any man ever will. They are almost absolutes, and each person must experience and master them to achieve the status of education. To some these three operations come easily, with little conscious effort. They sing as the bird sings, naturally. But to others (and here the subject becomes complicated), the opposite is true. Spelling is torture, reading is laborious and writing is almost impossible. They are different, and no one yet has precisely defined what their differences are. The problem is not due to lack of intellect. It may have something to do with attitude. It is certainly related to emotion, and in all probability it begins to manifest itself in the first three to five grades; often this "difference" is not recognized. Often it lies latent, remaining unobserved, until later, when it rears its ugly head in the form of severe learning difficulties and academic distress. Parents are horrified, teachers are nonplused, and the student suffers.

The results of this disorder may be severe. Some students, with good minds, become discouraged and quit. Some struggle on, laboring under great handicaps. Others seek help in the form of remedial exercises and tutoring. This group is perhaps the most fortunate because already an increasing number of

experts can offer them help in such a way that the final result may be academic success instead of failure. This knowledge is therapeutic and prophylactic and may be compared to similar procedures in various branches of medicine and related sciences. This is a new branch of knowledge, not widely advertised nor yet fully proved, but it is growing in use and becoming more systematic each day. Essentially, however, it has some features of an art, and those who practice it successfully are not unlike artists in their methodology, or lack of methodology. Most of them are optimists, and some are inspired. They accept heavy burdens and carry them cheerfully. Their attitude in this labor may be compared to that of the pioneers in medical science, to whom, through psychology, they are somehow related.

Two pioneers in this field and outstanding practitioners of remedial work in the learning process have contributed an article to this issue of the *Journal* that may prove useful and worthwhile reading to the physician who is interested in the whole personality of his patients and especially to family physicians to whom parents come first complaining: "Why can't Junior get along better in school? He seems bright enough, but he can't spell and he has trouble reading." In fact this was exactly what was said about Darwin and Einstein when they were young. But, somehow, they overcame it. Today, pupils with reading and spelling problems have an even better chance, thanks to the workers in the field of remedial reading and tutoring.

RING OUT, WILD BELLS

THE Direct Mail Advertising Association, Inc., in its Newsletter of January 1, 1955, (a new year — and a new masthead) announced to a waiting world that International Printing Week would be celebrated January 16 to 22 in more than a hundred cities of the United States and Canada, from sea to shining sea. Either certain special weeks were omitted, however, or January the destitute fares badly in comparison with February the abundant in the matter of having its days and weeks really assigned to the uplifting of mankind.

The special observances listed on the February calendar have required some doubling up and in one case quadruplication of interests; so many players have crowded the course that starting times have had to be designated and some intriguing combinations have resulted.

It will be noted that February 2 and 28, on the February Promotion Calendar presented below, had been unassigned at the time of publication either as special days or as parts of special weeks; it seems inconceivable that they might be left as barren days except for their inclusion in American Heart Month — or perhaps some worthy enterprises have stepped in to fill these gaps since the Newsletter went to press:

FEBRUARY	EVENT
1-28	American Heart Month
1	National Freedom Day
5-12	Kraut and Frankfurter Week
5-14	National Pimiento Week
6-12	Boy Scout Week
6-12	National Table Tennis Week
7	National Children Dental Health Day
12-22	Americanism Week
12-22	National Defense Week
13	Race Relations Sunday
13-19	National Advertising Week
13-19	National Crime Prevention Week
15-22	National Cherry Week
19-26	National Sew and Save Week
20-26	National Beauty Salon Week
20-26	Catholic Book Week
20-26	National Engineer's Week
20-27	Brotherhood Week
22	Pancake Day
25	World Day of Prayer

This apparent popularity of February renders the proposed World Calendar all the more desirable, giving to the short winter month two days more, or perhaps every year should be leap year; or does February present only a fair sample of the joyous burden that each month bears?

FROM THE BOOKS OF —

THE personal bookplate, which an irreverent age might facetiously and certainly erroneously characterize as the hallmark of a gentleman who wished to be considered a scholar (or vice versa), is nearly as old as the printed book itself. Originating in Germany as early as the fifteenth century, the *ex libris* appeared as a separate label to be pasted into individual volumes to indicate ownership. The particular plate that was, according to certain authorities, the progenitor of all bookplates, consisted of a woodcut representing a shield of arms supported by angels; it was found pasted into books presented in 1480 to the Carthusian monastery of Buxheim by Brother Hildebrand Brandenburg.

The Brandenburg claims for priority in the use of so-called movable bookplates are challenged by other authorities, however, in favor of the plate of Johannes Knabensberg, chaplain of the family of Schönstett. This plate, also from a woodcut, is said to have been found in an old Latin vocabulary about 1450. Albrecht Dürer engraved at least six of the early Ger-

man plates between 1503 and 1516, and the elaborate style of the period, established by Dürer, Holbein and others, with plates at one time colored by hand, set a fashion in design that is still current.

The custom of personalizing one's library through the use of bookplates spread gradually to the other countries of Europe; the first distinctly American plate is that of John Cotton, consisting of a simple printed label — "John Cotton his Book Ann. Dom. 1674." It is as unequivocal as "Keep off the Grass." The plate of Paul Revere, not surprisingly, was capably engraved about the year 1775. It depicts a lion squatted on his heels supporting and supported by a shield bearing the motto *Pugna pro Patria,* liberally translatable, perhaps, as "Pugnacious for the Fatherland."

The term *ex libris,* used as a substantive, is the acknowledged synonym for "bookplate" on the continent of Europe, according to no less an authority than the *Encyclopaedia Britannica.* It was not until after the mid-seventeenth century that the movable *ex libris* became common in France, and many of the most dignified and artistic plates originated in that country.

English bookplates, of limited popularity until the latter part of the seventeenth century, are generally more simply executed than their German counterparts. They are frequently armorial in design; otherwise they may be grouped according to subject, whether library interiors, bookpiles, portraits, allegories or landscapes. Becoming elaborate for a time during the early Georgian period, they have followed in general the prevailing taste in decorative art.

The collecting of bookplates and the value attached to them as collector's items is of comparatively recent origin. Societies of collectors have come into being, and the literature of the subject is relatively extensive, with a number of books, journals and archives devoted to it. One of the early works of note, *Guide to the Study of Book-Plates,* by the Honorable Leicester Warren, later Lord de Tabley, was published in 1880.

The Boston Medical Library has in its possession a substantial collection of medical bookplates, some of which will be reproduced in these pages from time to time. Its own official plate, as the first of the series, appears elsewhere in this issue of the *Journal.* Included are plates that have been designed especially for the books purchased from special funds, and many personal bookplates, a number of them of considerable interest, identify the private book collections that have been left to the Library.

BILL OF RIGHTS

As of present date the 1955 Heart Fund appeal, taking place throughout February, is well under way with its high point falling on February 20, designated as Heart Sunday. General Mark Clark and Dr. E. Cowles Andrus, president of the American Heart Association, head the national campaign, and O. Kelley Anderson, president of the New England Mutual Life Insurance Company, Inc., and Dr. Robert W. Wilkins, president of the Massachusetts Heart Association, are in charge of the state appeal.

The Association emphasizes certain important points in its fact sheet. The funds received as a result of the campaign are divided into three parts of which 60 per cent remains in the local chapter treasury, 25 per cent goes to the national body, of which a minimum of half is allocated to research, and 15 per cent goes to the Massachusetts Association for research and program development.

It is further emphasized that no local or national goal for the appeal has been set; that in the opinion of both the state and the national associations a gift should be voluntary and a donor should have the right to select the causes that he wishes to support. In other words, a person's right not to give is considered by the associations as important as his right to give.

A bill has been introduced into the New York Assembly, to incorporate P. T. Barnum and others into a Hydropathic Medical College, with powers to confer the degree of Doctor of Medicine. Some remarks on this subject will appear in our next.

Boston M. & S. J., *Feb. 15, 1855*

MASSACHUSETTS MEDICAL SOCIETY

DEATH

SCHLESINGER — Monroe J. Schlesinger, M.D., of Newton Center, died on January 20. He was in his sixty-third year.

Dr. Schlesinger received his degree from Harvard Medical School in 1926. He was clinical professor of pathology, Harvard Medical School, and consultant in pathology, Beth Israel Hospital, a fellow of the College of American Pathologists and the American Medical Association, a member of the American Association of Pathologists and Bacteriologists, American Society for Experimental Pathology and Society of American Bacteriologists and, formerly, president of the New England Pathological Society and a councilor of the Massachusetts Medical Society.

He is survived by his widow, daughter, son and sister.

CORRESPONDENCE

BULLETIN OF CANCER PROGRESS

To the Editor: As most physicians know, a *free* subscription to *CA — A Bulletin of Cancer Progress* is made available by the Massachusetts Division of the American Cancer Society to any licensed physician who requests it. If any Massachusetts physician is interested in this bulletin, a request should be made promptly by mail or telephone to the address shown.

CLARENCE L. SCAMMAN, M.D.
Medical Director
American Cancer Society
(Massachusetts Division), Inc.
Boston

NOTICES

PHARMACOLOGY SEMINAR

A pharmacology seminar under the auspices of Harvard Medical School, Tufts College Medical School and Boston University School of Medicine will be held in the auditorium, Building A, Boston University School of Medicine, on March 2 at 4:30 p.m.

Dr. René Wegria, College of Physicians and Surgeons, Columbia University, will discuss the topic "Pharmacology of the Coronary Circulation."

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next scheduled oral and clinical examinations (Part II) for all candidates for the American Board of Obstetrics and Gynecology will be held at the Edgewater Beach Hotel, Chicago, May 12 through 20.

Formal notice of the time of the examination for each candidate will be sent to him in advance of the dates of the examination. Case abstracts must be in the office of the secretary, Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio, before February 28 if not already submitted.

SOCIETY MEETINGS AND CONFERENCES

FEBRUARY–APRIL. Postgraduate Medical Institute. Page 451, issue of September 9.

FEBRUARY–MAY. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.

FEBRUARY 10–23. Consultation Clinics for Crippled Children in Massachusetts. Page 155, issue of January 27.

FEBRUARY 11 and 12. International College of Surgeons. Page 157, issue of January 27.

FEBRUARY 11–25. Pan-American Academy of General Practice. Page 496, issue of September 16.

FEBRUARY 11–MARCH 25. Postgraduate Course in Occupational Medicine. Page 922, issue of November 25.

FEBRUARY 14–MAY 9. Seminar in Psychiatry and Neurology. Page 452, issue of September 9.

FEBRUARY 15. Tufts Medical Alumni Association Lecture. Page 157, issue of January 27.

FEBRUARY 15. New England Deaconess Hospital Lectures. Page 993, issue of December 9.

FEBRUARY 15. South End Medical Society. Page 202, issue of February 3.

FEBRUARY 15. Framingham General Hospital Lecture. Page 201, issue of February 3.

FEBRUARY 26 and 27. Mid-Winter Radiologic Conference. Page 1076, issue of December 23.

FEBRUARY 28–MARCH 1. International College of Surgeons, Southwestern Division Regional Meeting. Page 157, issue of January 27.

FEBRUARY 28–MARCH 2. American Orthopsychiatric Association. Page 994, issue of December 9.

MARCH 2. Pharmacology Seminar. Notice above.

MARCH 5–MAY 7. Middlesex South District Medical Society. Postgraduate Course. Page 758, issue of October 28.

MARCH 7–12. Course in Care of Atomic Casualties. Page 285, issue of August 12.

MARCH 20–23. Aero Medical Association. Page 157, issue of January 27.

MARCH 23–26. International Academy of Proctology. Page 876, issue of November 18.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 17

THURSDAY, FEBRUARY 17

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Yamins A, Beth Israel Hospital.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Thoracic Conference. Hydraulics of Thoracic Surgery. Dr. Warren Taylor. Main Amphitheater, Peter Bent Brigham Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m.–1:00 p.m. Surgical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*12:00 m.–1:30 p.m. Boston City Hospital Teaching Conference. Essential Hypertension in Pregnancy. Dr. Laurence B. Ellis. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:15–1:15 p.m. Tumor Clinic. Amphitheater, Peter Bent Brigham Hospital.
*4:00–5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

FRIDAY, FEBRUARY 18

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Dr. Proger and Staff. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00–5:00 p.m. Child Psychiatry. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

SATURDAY, FEBRUARY 19

*8:00 a.m. Gynecological Grand Rounds. 6th-floor conference room. Carney Hospital, 2100 Dorchester Avenue, Dorchester.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

MONDAY, FEBRUARY 21

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Metabolism Conference. Dr. Schwartz. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Pediatric Medical-Surgical Rounds. Drs. Baty and Swenson. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:00 p.m. Surgical Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.

TUESDAY, FEBRUARY 22

Holiday

WEDNESDAY, FEBRUARY 23

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00–10:00 a.m. Surgical Grand Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*12:00 m. Boston State Hospital. Psychiatry Seminar. Allergic Disorders. Dr. Francis M. Rackemann. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th-floor teaching unit, Beth Israel Hospital.
*12:00 m.–1:00 p.m. Neurology, Neurosurgery and Psychiatry Conference. Drs. Sullivan, B. Selverstone and Hope. Stearns Auditorium, New England Center Hospital.
*12:15 p.m. Vascular Rounds. Drs. Edward A. Edwards and Chilton Crane. D-Main, Peter Bent Brigham Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. The Clinics of the Massachusetts General Hospital.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. The Place of Physiological Studies in Pulmonary Tuberculosis. Dr. Giles Filley. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*7:30–9:30 p.m. Lahey Clinic Lecture. Joslin Auditorium, New England Deaconess Hospital.

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*L. J. Cass et al., *New England J. Med.*, 249:132, 1953; *Am. J. M. Sc.*, 227:291, 1954.

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1. Suarez-Murias, E. L.: Internat. Rec. Med. *166:*475 (Nov.) 1953. 2. Rees, L.: J. Ment. Sc. *99:*62 (Jan.) 1953. 3. Morton, J. H., et al.: Am. J. Obst. & Gynec. *65:*1182 (June) 1953. 4. Morton, J. H.: Internat. Rec. Med. *166:*505 (Nov.) 1953.

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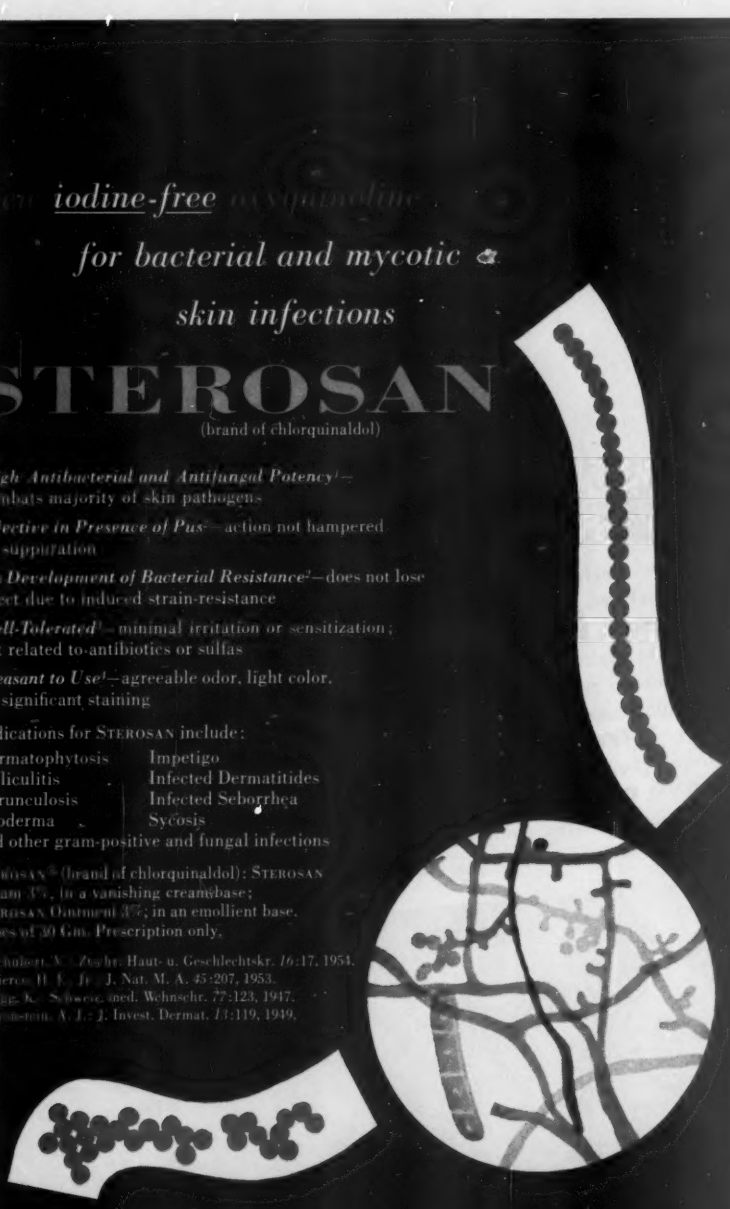

1. Schubert, V.: Ztschr. Haut- u. Geschlechtskr. *16*:17, 1954.
2. Pierce, H. F., Jr.: J. Nat. M. A. *45*:207, 1953.
3. Sigg, K.: Schweiz. med. Wchnschr. *77*:123, 1947.
4. Tronstein, A. J.: J. Invest. Dermat. *13*:119, 1949.

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1. McHardy and Browne: Sou. Med. J. 45:1139, 1952. 2. Lorber and Shay: Fed. Proc. 12:90, 1952.

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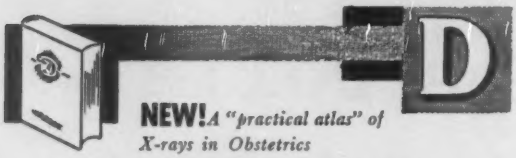

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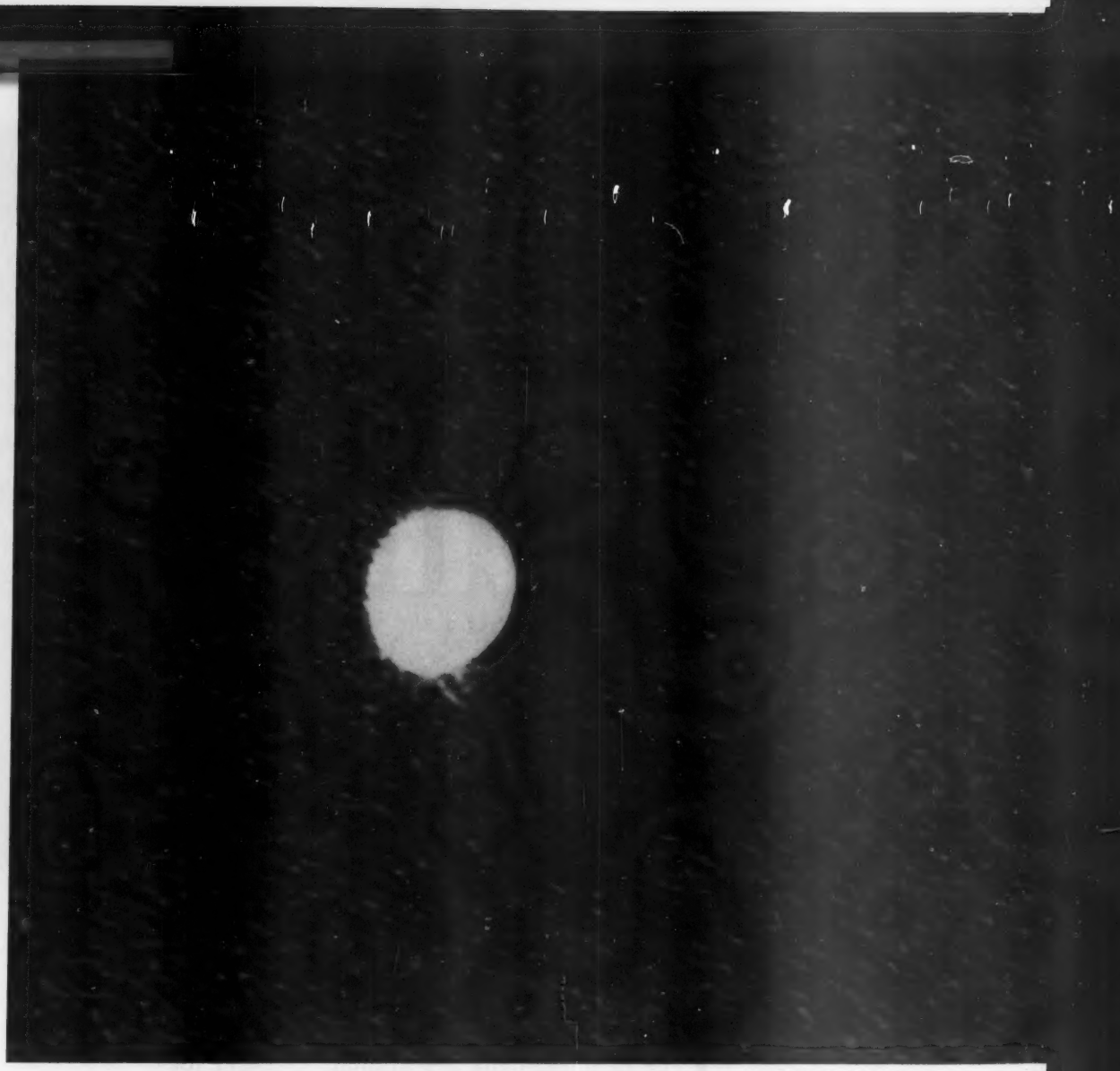

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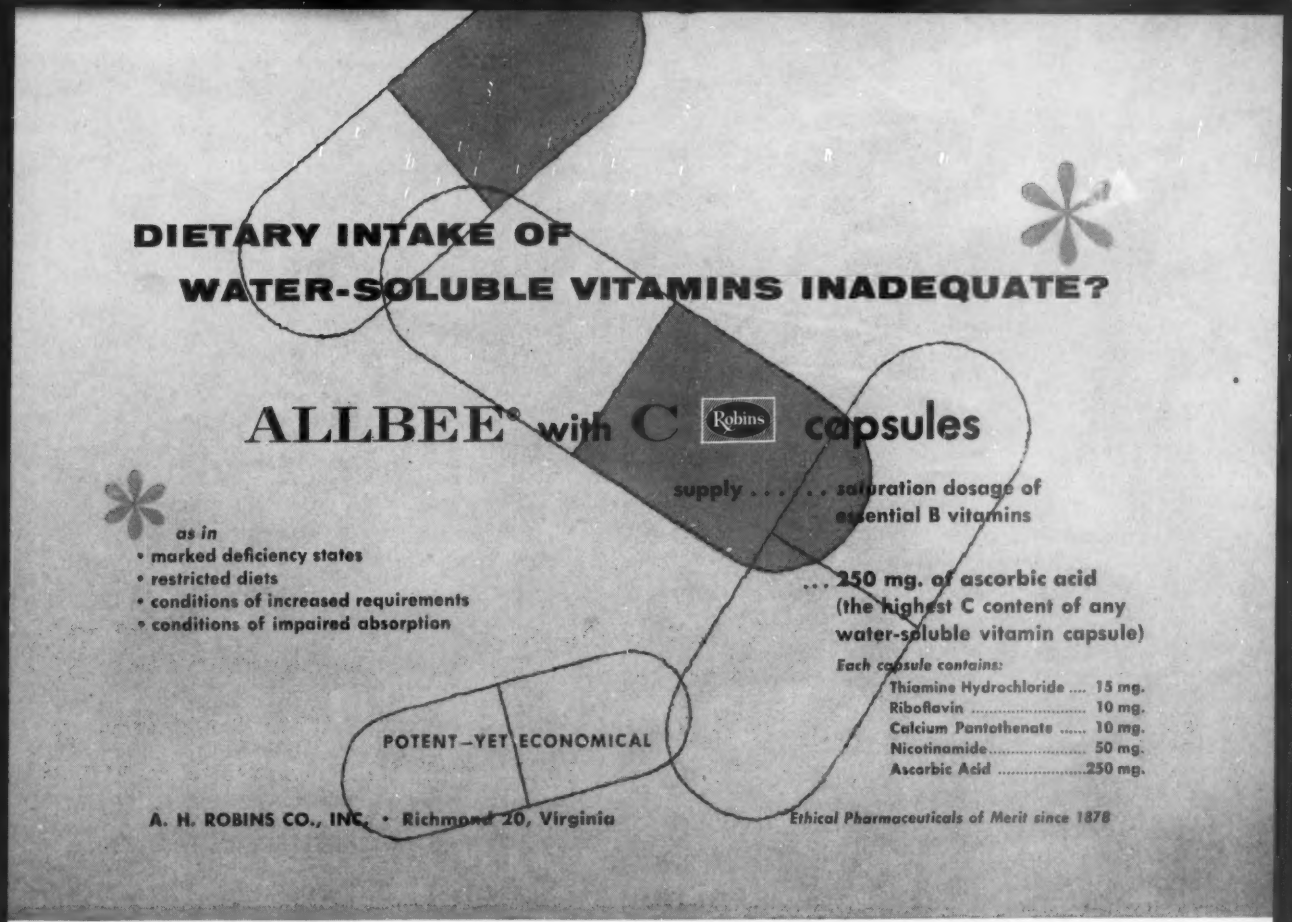
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